```
=> file registry
FILE 'REGISTRY' ENTERED AT 17:01:21 ON 26 OCT 2005
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   25 OCT 2005  HIGHEST RN 866083-87-6
DICTIONARY FILE UPDATES:  25 OCT 2005  HIGHEST RN 866083-87-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*************************************************************************
*                                                                       *
* The CA roles and document type information have been removed from     *
* the IDE default display format and the ED field has been added,       *
* effective March 20, 2005.  A new display format, IDERL, is now        *
* available and contains the CA role and document type information.     *
*                                                                       *
*************************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d stat que L4
L2                STR
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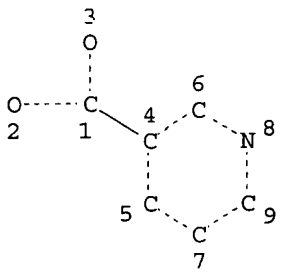


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   9
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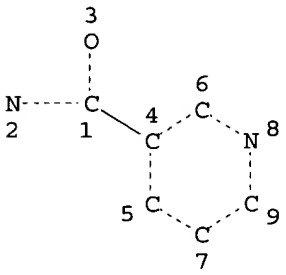
STEREO ATTRIBUTES: NONE
L4 745 SEA FILE=REGISTRY FAM FUL L2

100.0% PROCESSED 9946 ITERATIONS 745 ANSWERS
SEARCH TIME: 00.00.01

Nicotinic acid family search

=> d stat que L8
L6 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

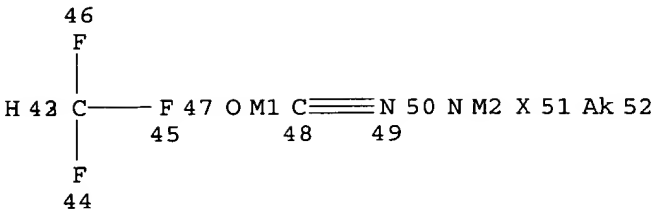
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

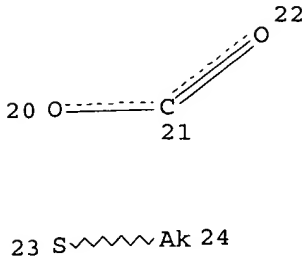
STEREO ATTRIBUTES: NONE
L8 387 SEA FILE=REGISTRY FAM FUL L6

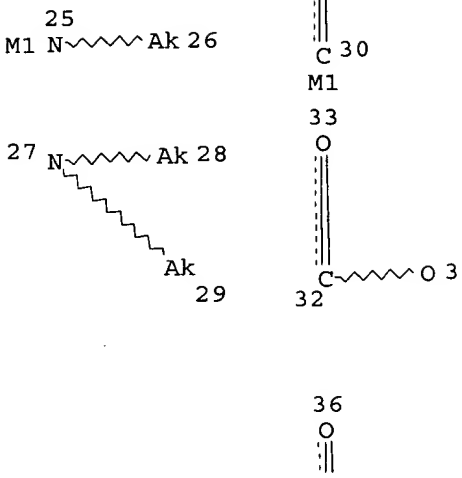
nicotinamide family search

100.0% PROCESSED 11587 ITERATIONS 387 ANSWERS
SEARCH TIME: 00.00.01

=> d stat que L11
L9 STR



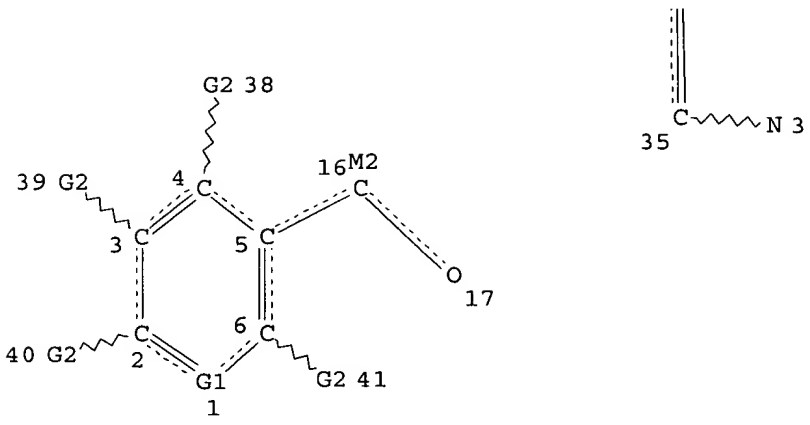


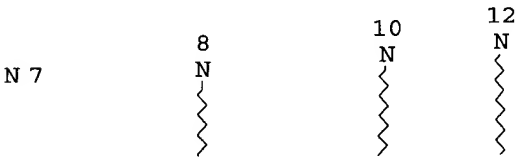


Page 1-A

4

Page 1-B

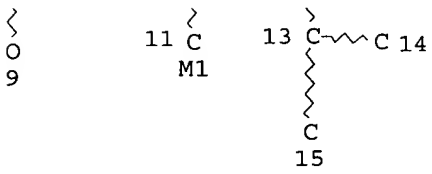




Page 2-A

7

Page 2-B



Page 3-A

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VAR G2=42/43/47/48/50/51/52/18/20/23/25/27/30/32/35
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HCOUNT	IS M2	AT	16
HCOUNT	IS M1	AT	25
HCOUNT	IS M1	AT	30
HCOUNT	IS M1	AT	47
HCOUNT	IS M2	AT	50
NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS R	AT	6
NSPEC	IS R	AT	7

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NSPEC   IS R       AT   8
NSPEC   IS C       AT   9
NSPEC   IS C       AT  10
NSPEC   IS C       AT  11
NSPEC   IS C       AT  12
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NSPEC   IS RC      AT  14
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NSPEC   IS C       AT  16
NSPEC   IS C       AT  17
NSPEC   IS C       AT  18
NSPEC   IS C       AT  19
NSPEC   IS C       AT  20
NSPEC   IS C       AT  21
NSPEC   IS C       AT  22
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NSPEC   IS C       AT  41
CONNECT IS E2  RC AT   7
CONNECT IS E1  RC AT   9
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
          26 27 28 29 30 31 32 33 34 35 36 37 42 43 44 45 46 47 48 49 50
          51 52
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  52

STEREO ATTRIBUTES: NONE
L11       11383 SEA FILE=REGISTRY SSS FUL L9

100.0% PROCESSED  601827 ITERATIONS                 11383 ANSWERS
SEARCH TIME: 00.00.09
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← structure search for drawn compounds

```
=> file caplus
FILE 'CAPLUS' ENTERED AT 17:04:52 ON 26 OCT 2005
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FILE COVERS 1907 - 26 Oct 2005 VOL 143 ISS 18
FILE LAST UPDATED: 25 Oct 2005 (20051025/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

AUTHOR SEARCH

=> d que L56

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L46          30 SEA FILE=CAPLUS ABB=ON  PLU=ON  BIEDERMANN E?/AU
L47          23 SEA FILE=CAPLUS ABB=ON  PLU=ON  HASMANN M?/AU
L48          31 SEA FILE=CAPLUS ABB=ON  PLU=ON  LOSER R?/AU
L49          16 SEA FILE=CAPLUS ABB=ON  PLU=ON  RATTEL B?/AU
L50         132 SEA FILE=CAPLUS ABB=ON  PLU=ON  REITER F?/AU
L51          18 SEA FILE=CAPLUS ABB=ON  PLU=ON  SCHEIN B?/AU
L52           9 SEA FILE=CAPLUS ABB=ON  PLU=ON  SCHEMAINDA I?/AU
L53          75 SEA FILE=CAPLUS ABB=ON  PLU=ON  SEIBEL K?/AU
L54         368 SEA FILE=CAPLUS ABB=ON  PLU=ON  VOGT K?/AU
L55          21 SEA FILE=CAPLUS ABB=ON  PLU=ON  WOSIKOWSKI K?/AU
L56           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L46 AND L47 AND L48 AND L49
                AND L50 AND L51 AND L52 AND L53 AND L54 AND L55
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=> d que L63

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L46          30 SEA FILE=CAPLUS ABB=ON  PLU=ON  BIEDERMANN E?/AU
L47          23 SEA FILE=CAPLUS ABB=ON  PLU=ON  HASMANN M?/AU
L48          31 SEA FILE=CAPLUS ABB=ON  PLU=ON  LOSER R?/AU
L50         132 SEA FILE=CAPLUS ABB=ON  PLU=ON  REITER F?/AU
L53          75 SEA FILE=CAPLUS ABB=ON  PLU=ON  SEIBEL K?/AU
L54         368 SEA FILE=CAPLUS ABB=ON  PLU=ON  VOGT K?/AU
L55          21 SEA FILE=CAPLUS ABB=ON  PLU=ON  WOSIKOWSKI K?/AU
L63           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L46 AND L47 AND L48 AND L50
                AND L53 AND L54 AND L55
```

=> d que L64

```
L49          16 SEA FILE=CAPLUS ABB=ON  PLU=ON  RATTEL B?/AU
L51          18 SEA FILE=CAPLUS ABB=ON  PLU=ON  SCHEIN B?/AU
L52           9 SEA FILE=CAPLUS ABB=ON  PLU=ON  SCHEMAINDA I?/AU
L64           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L49 AND L51 AND L52
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=> s L56 or L63 or L64

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L213          6 L56 OR L63 OR L64
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=> file medline

FILE 'MEDLINE' ENTERED AT 17:04:56 ON 26 OCT 2005

 FILE LAST UPDATED: 25 OCT 2005 (20051025/UP). FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available. For details enter HELP
 RLOAD at an arrow promt (=>). See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que L146

L136          3 SEA FILE=MEDLINE ABB=ON  PLU=ON  BIEDERMANN E?/AU
L137         14 SEA FILE=MEDLINE ABB=ON  PLU=ON  HASMANN M?/AU
L138         44 SEA FILE=MEDLINE ABB=ON  PLU=ON  LOSER R?/AU
L139          8 SEA FILE=MEDLINE ABB=ON  PLU=ON  RATTEL B?/AU
L140         26 SEA FILE=MEDLINE ABB=ON  PLU=ON  REITER F?/AU
L141         13 SEA FILE=MEDLINE ABB=ON  PLU=ON  SCHEIN B?/AU
L142          5 SEA FILE=MEDLINE ABB=ON  PLU=ON  SCHEMAINDA I?/AU
L143         43 SEA FILE=MEDLINE ABB=ON  PLU=ON  SEIBEL K?/AU
L144        162 SEA FILE=MEDLINE ABB=ON  PLU=ON  VOGT K?/AU
L145         16 SEA FILE=MEDLINE ABB=ON  PLU=ON  WOSIKOWSKI K?/AU
L146          0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L136 AND L137 AND L138 AND
                L139 AND L140 AND L141 AND L142 AND L143 AND L144 AND L145


=> d que L152

L136          3 SEA FILE=MEDLINE ABB=ON  PLU=ON  BIEDERMANN E?/AU
L137         14 SEA FILE=MEDLINE ABB=ON  PLU=ON  HASMANN M?/AU
L138         44 SEA FILE=MEDLINE ABB=ON  PLU=ON  LOSER R?/AU
L139          8 SEA FILE=MEDLINE ABB=ON  PLU=ON  RATTEL B?/AU
L140         26 SEA FILE=MEDLINE ABB=ON  PLU=ON  REITER F?/AU
L141         13 SEA FILE=MEDLINE ABB=ON  PLU=ON  SCHEIN B?/AU
L142          5 SEA FILE=MEDLINE ABB=ON  PLU=ON  SCHEMAINDA I?/AU
L143         43 SEA FILE=MEDLINE ABB=ON  PLU=ON  SEIBEL K?/AU
L144        162 SEA FILE=MEDLINE ABB=ON  PLU=ON  VOGT K?/AU
L145         16 SEA FILE=MEDLINE ABB=ON  PLU=ON  WOSIKOWSKI K?/AU
L149          2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L136 AND ((L137 OR L138 OR
                L139 OR L140 OR L141 OR L142 OR L143 OR L144 OR L145))
L150         19 SEA FILE=MEDLINE ABB=ON  PLU=ON  L149 OR ((L137 AND ((L138 OR
                L139 OR L140 OR L141 OR L142 OR L143 OR L144 OR L145))) OR
                (L138 AND ((L139 OR L140 OR L141 OR L142 OR L143 OR L144 OR
                L145))))
L151          3 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L139 AND ((L140 OR L141 OR
                L142 OR L143 OR L144 OR L145))) OR (L140 AND ((L141 OR L142 OR
                L143 OR L144 OR L145))) OR (L141 AND ((L142 OR L143 OR L144 OR
```

```
                L145))) OR (L142 AND ((L143 OR L144 OR L145))) OR (L143 AND
                (L144 OR L145)) OR (L144 AND L145)
L152          19 SEA FILE=MEDLINE ABB=ON  PLU=ON  L150 OR L151


=> s L146 or L152

L214         19 L146 OR L152

=> file embase

FILE 'EMBASE' ENTERED AT 17:04:59 ON 26 OCT 2005
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 FILE COVERS 1974 TO 20 Oct 2005 (20051020/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> d que L165

L153           5 SEA FILE=EMBASE ABB=ON  PLU=ON  BIEDERMANN E?/AU
L154          16 SEA FILE=EMBASE ABB=ON  PLU=ON  HASMANN M?/AU
L155          30 SEA FILE=EMBASE ABB=ON  PLU=ON  LOSER R?/AU
L156           9 SEA FILE=EMBASE ABB=ON  PLU=ON  RATTEL B?/AU
L157          16 SEA FILE=EMBASE ABB=ON  PLU=ON  REITER F?/AU
L158           5 SEA FILE=EMBASE ABB=ON  PLU=ON  SCHEIN B?/AU
L159           4 SEA FILE=EMBASE ABB=ON  PLU=ON  SCHEMAINDA I?/AU
L160          52 SEA FILE=EMBASE ABB=ON  PLU=ON  SEIBEL K?/AU
L161         166 SEA FILE=EMBASE ABB=ON  PLU=ON  VOGT K?/AU
L162          16 SEA FILE=EMBASE ABB=ON  PLU=ON  WOSIKOWSKI K?/AU
L163          22 SEA FILE=EMBASE ABB=ON  PLU=ON  (L153 AND ((L154 OR L155 OR
                 L156 OR L157 OR L158 OR L159 OR L160 OR L161 OR L162))) OR
                 (L154 AND ((L155 OR L156 OR L157 OR L158 OR L159 OR L160 OR
                 L161 OR L162))) OR (L155 AND ((L156 OR L157 OR L158 OR L159 OR
                 L160 OR L161 OR L162))) OR (L156 AND ((L157 OR L158 OR L159 OR
                 L160 OR L161 OR L162)))
L164           1 SEA FILE=EMBASE ABB=ON  PLU=ON  (L157 AND ((L158 OR L159 OR
                 L160 OR L161 OR L162))) OR (L158 AND ((L159 OR L160 OR L161 OR
                 L162))) OR (L159 AND ((L160 OR L161 OR L162))) OR (L160 AND
                 ((L161 OR L162))) OR (L161 AND L162)
L165          22 SEA FILE=EMBASE ABB=ON  PLU=ON  L163 OR L164


=> => dup rem L213 L214 L165
FILE 'CAPLUS' ENTERED AT 17:06:12 ON 26 OCT 2005
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FILE 'MEDLINE' ENTERED AT 17:06:12 ON 26 OCT 2005

FILE 'EMBASE' ENTERED AT 17:06:12 ON 26 OCT 2005
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PROCESSING COMPLETED FOR L213
PROCESSING COMPLETED FOR L214
PROCESSING COMPLETED FOR L165
L215          30 DUP REM L213 L214 L165 (17 DUPLICATES REMOVED)
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ANSWERS '1-6' FROM FILE CAPLUS
ANSWERS '7-25' FROM FILE MEDLINE
ANSWERS '26-30' FROM FILE EMBASE

printout on next page →

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=> => d L215 ibib abs hitind 1-6; d iall 7-30 L215
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, CAPLUS, MEDLINE' - CONTINUE? (Y)/N:y

L215 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:706352 CAPLUS
DOCUMENT NUMBER: 133:276324
TITLE: Inhibitors of cellular nicotinamide mononucleotide formation, therapeutic use thereof, and identification and metabolic methods
INVENTOR(S): **Biedermann, Elfi**; Eisenburger, Rolf; **Hasmann, Max**; **Loser, Roland**; **Rattel, Benno**; **Reiter, Friedemann**; **Schein, Barbara**; **Schemainda, Isabel**; Schulz, Michael; **Seibel, Klaus**; **Vogt, Klaus**; **Wosikowski, Katja**
PATENT ASSIGNEE(S): Klinge Pharma G.m.b.H., Germany
SOURCE: Ger. Offen., 20 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908483	A1	20001005	DE 1999-19908483	19990226
PRIORITY APPLN. INFO.:			DE 1999-19908483	19990226

AB Biol. active substances are described which inhibit the cellular formation of NMN, an essential intermediate in NAD(P) biosynthesis in the cell. These substances can be used for a pharmaceutical composition for the treatment of cancer, leukemia, or for Immunosuppression. Addnl., methods are described for the identification of such substances and for the investigation of a given cell type for its dependence on nicotinamide as a precursor in NAD synthesis.

IC ICM C07D401-12
ICS C07D401-14; C07D213-24; C07D295-185; C12Q001-02; A61K031-4406
CC 1-6 (Pharmacology)
Section cross-reference(s): 9, 63
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:690954 CAPLUS
DOCUMENT NUMBER: 131:307106
TITLE: Use of vitamin PP compounds as cytoprotective agents in chemotherapy
INVENTOR(S): **Biedermann, Elfi**; **Hasmann, Max**; **Loser, Roland**; **Rattel, Benno**; **Reiter, Friedemann**; **Schein, Barbara**; **Schemainda, Isabel**; **Seibel, Klaus**; **Vogt, Klaus**; **Wosikowski, Katja**
PATENT ASSIGNEE(S): Klinge Pharma GmbH, Germany
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953920	A1	19991028	WO 1999-EP2686	19990421
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19818044	A1	19991028	DE 1998-19818044	19980422
EP 1031564	A1	20000830	EP 1999-103814	19990226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9939282	A1	19991108	AU 1999-39282	19990421
EP 1079832	A1	20010307	EP 1999-922119	19990421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002512190	T2	20020423	JP 2000-544324	19990421
WO 2000050399	A1	20000831	WO 2000-EP1628	20000228
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1154998	A1	20011121	EP 2000-907642	20000228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537380	T2	20021105	JP 2000-600982	20000228
US 2002160968	A1	20021031	US 2001-935772	20010823
US 6506572	B2	20030114		

PRIORITY APPLN. INFO.:	DE 1998-19818044	A	19980422
	EP 1999-103814	A	19990226
	WO 1999-EP2686	W	19990421
	WO 2000-EP1628	W	20000228

OTHER SOURCE(S): MARPAT 131:307106

AB The invention relates to the use of vitamin PP compds. and/or compds. with anti-pellagra activity such as for example nicotinic acid (niacin), and nicotinamide (niacin-amide, vitamin PP, vitamin B3) for the reduction, elimination or prevention of side-effects of different degrees as well as for neutralization of acute side-effects in immunosuppressive or cancerostatic chemotherapy or diagnosis, especially with substituted pyridine carboxamides, as well as combination medicaments with an amount of compds. with vitamin B3 and/or anti-pellagra activity and chemotherapeutic agents are especially considered in the mentioned chemotherapies and indications. Nicotinamide at 500 mg/kg twice daily protected mice treated i.p. with antitumor N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide. There were no deaths in the nicotinamide-treated mice and the strong reduction of leukocytes was completely prevented.

IC ICM A61K031-455
ICS A61K031-465; A61K031-44; A61K031-455; A61K031-44; A61K031-465; A61K031-44

CC 1-12 (Pharmacology)

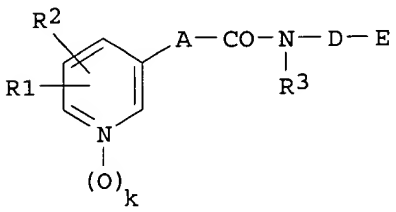
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

L215 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:404952 CAPLUS
DOCUMENT NUMBER: 131:58758
TITLE: Cyclic imide-substituted pyridylalkanecarboxamides, pyridylalkenecarboxamides and pyridylalkynecarboxamides useful as cytostatic and immunosuppressive agents
INVENTOR(S): **Biedermann, Elfi**; **Hasmann, Max**; **Loser, Roland**; Rattel, Benno; **Reiter, Friedemann**; Schein, Barbara; **Seibel, Klaus**; **Vogt, Klaus**; **Wosikowski, Katja**
PATENT ASSIGNEE(S): Klinge Pharma G.m.b.H., Germany
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931087	A1	19990624	WO 1998-EP8267	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19756212	A1	19990701	DE 1997-19756212	19971217
ZA 9811231	A	19990608	ZA 1998-11231	19981208
AU 9924146	A1	19990705	AU 1999-24146	19981216
EP 1042315	A1	20001011	EP 1998-966634	19981216
EP 1042315	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508367	T2	20020319	JP 2000-539011	19981216
AT 264321	E	20040415	AT 1998-966634	19981216
PT 1042315	T	20040831	PT 1998-966634	19981216
ES 2218881	T3	20041116	ES 1998-966634	19981216

PRIORITY APPLN. INFO.: DE 1997-19756212 A 19971217
WO 1998-EP8267 W 19981216

OTHER SOURCE(S): MARPAT 131:58758
GI



AB Pyridine derivs. I [R1 = H, OH, halo, CN, or organic group; R2 = H, halo, CN, alkyl, trifluoromethyl, OH, alkoxy, or aralkoxy; R3 = H, alkyl, alkenyl, alkynyl, OH, alkoxy, or aryloxy; A = (substituted) alkylene, 1,2-cyclopropylene, (substituted) alkenylene, (substituted) alkadienylene, (substituted) hexatrienylene, or ethynylene; D = (substituted) alkylene, (substituted) alkenylene, (substituted) alkynylene (in which 1-3 CH2 units is isosterically replaced by O, S, NR4, CO, SO, or SO2, R4 = H, alkyl, alkenyl, acyl, or alkanesulfonyl); E = N-substituted cyclic imide or N-substituted cyclic sulfonimide; k = 0 or 1] are manufactured for use as cytostatic agents and immunosuppressive agents. Thus, slowing adding 46.9 mmol oxalyl chloride to 20 mmol 3-(3-pyridyl)acrylic acid suspended in CH2Cl2, stirring the mixture with ice-cooling for 30 min and then at room temperature overnight, suspending the resulting acid chloride in CH2Cl2, cooling to 0° under anhydrous conditions, adding 17.6 mmol 4-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)butylamine-HCl in CH2Cl2 and 39.5 mmol Et3N dropwise, and stirring an addnl. 2 h at room temperature gave N-[4-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)butyl]-3-pyridin-3-ylacrylamide.

IC ICM C07D401-12
ICS C07D417-12; C07D409-14; C07D401-14; C07D417-14; A61K031-44

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 28, 63

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

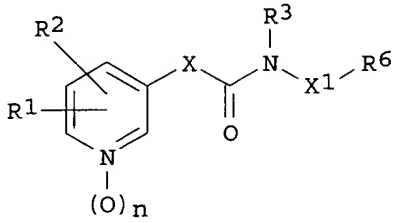
L215 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:404933 CAPLUS
DOCUMENT NUMBER: 131:58757
TITLE: Aryl-substituted pyridyl alkane, alkene, and alkyne carboxamides useful as cytostatic and immunosuppressive agents
INVENTOR(S): **Biedermann, Elfi**; **Hasmann, Max**; **Loser, Roland**; Rattel, Benno; **Reiter, Friedemann**; Schein, Barbara; **Seibel, Klaus**; **Vogt, Klaus**; **Wosikowski, Katja**
PATENT ASSIGNEE(S): Klinge Pharma G.m.b.H., Germany
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931064	A1	19990624	WO 1998-EP8272	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19756261	A1	19990701	DE 1997-19756261	19971217
ZA 9811240	A	19990608	ZA 1998-11240	19981208

AU 9922740	A1	19990705	AU 1999-22740	19981216
EP 1042291	A1	20001011	EP 1998-966352	19981216
EP 1042291	B1	20050713		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508357	T2	20020319	JP 2000-538991	19981216
AT 299495	E	20050715	AT 1998-966352	19981216
PRIORITY APPLN. INFO.:			DE 1997-19756261	A 19971217
			WO 1998-EP8272	W 19981216

OTHER SOURCE(S): MARPAT 131:58757

GI



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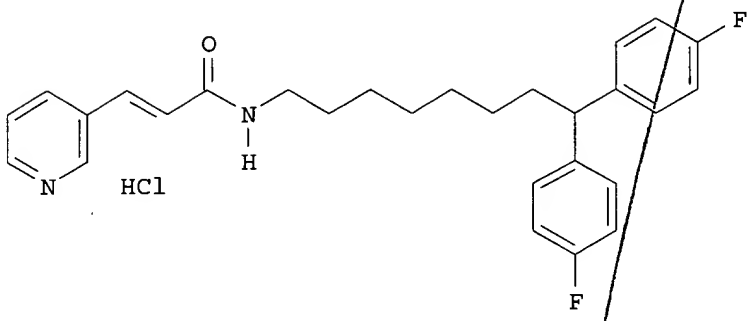

II

AB The pyridine-containing carboxamides I [n = 0, 1; R1 = H, halo, cyano, alkyl, alkenyl, alkynyl, alkoxy, HO, H2NCO, alkylthio, PhO, pyridyloxy, R4R5N (R4, R5 = H, alkyl, alkenyl, alkynyl, aralkyl, aryl), etc.; R2 = H, halo, cyano, alkyl, fluoroalkyl, HO, alkoxy, PhCH2O, etc.; R3 = H, alkyl, alkenyl, alkynyl, HO, alkoxy, aralkyloxy, etc.; X = alkylene substituted by alkyl, HO, alkoxy, F, aryl; alkylene with methylene unit isosterically replaced by O, S, NH, substituted NH, CO, SO, SO2; 1,2-cyclopropylene, alkenylene, alkadienylene, hexatrienylene, ethynylene; X1 = substituted alkylene, alkenylene, alkynylene, and alkylene, alkenylene, or alkynylene with methylene units replaced by O, S, NH, substituted NH, CO, SO, or SO2; R6 = R7(CR8R9)m; m = 0, 1; R7 = aralkyl, heterocyclyl , carbocyclyl, R8, R9 = H, HO, alkyl alkenyl, alkynyl, cycloalkyl, aralkyl, etc.; R6 = R8R9C:; R8, R9 = as above or R8R9C: = carbocyclic or heterocyclic ring system bound over the C atom; R6 = R7(CR8R9)m-(CH2)p-X2; R7, R8, R9, m as above; p = 1-2; X2 = substituted NH, O, S; R6 = NR8R9, R8, R9 as above or NR8R9 = N-heterocyclyl ; R6 = R7(CR8R9)m-X3-CONH-; R7, R8, R9, m as above, X3 = bond, methylene, ethylene, cycloalkylene, etc.; R6 = substituted sulfonylamino; R6 = Ar(Ar1)P(O)-; Ar, Ar1 = aryl, heteroaryl] were prepared for use as cytostatic and immunosuppressive agents. Thus, 3-(3-pyridinyl)acrylic acid was chlorinated with oxalyl chloride and then amidated with (4-FC6H4)2CH(CH2)7NH2 to give the N-octylacrylamide II which

inhibited HepG2 cells from a human liver carcinoma with IC50 = 0.05 μM.
IC ICM C07D213-56
ICS C07D401-12; C07D417-12; C07D409-12; C07D413-12; C07D409-14; C07D405-12; C07D491-04; C07D495-04; A61K031-44
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:404932 CAPLUS
DOCUMENT NUMBER: 131:58849
TITLE: New piperazinyl-substituted pyridylalkane, -alkene, and -alkyne carboxamides, with antitumor and immunosuppressive activities
INVENTOR(S): **Biedermann, Elfi**; **Hasmann, Max**; **Loser, Roland**; Rattel, Benno; **Reiter, Friedemann**; Schein, Barbara; **Seibel, Klaus**; **Vogt, Klaus**; **Wosikowski, Katja**
PATENT ASSIGNEE(S): Klinge Pharma G.m.b.H., Germany
SOURCE: PCT Int. Appl., 224 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931063	A1	19990624	WO 1998-EP8268	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19756236	A1	19990701	DE 1997-19756236	19971217
ZA 9811235	A	19990608	ZA 1998-11235	19981208
AU 9920543	A1	19990705	AU 1999-20543	19981216
EP 1060163	A1	20001220	EP 1998-965275	19981216
EP 1060163	B1	20051012		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508356	T2	20020319	JP 2000-538990	19981216
US 6903118	B1	20050607	US 2000-596001	20000616
PRIORITY APPLN. INFO.:			DE 1997-19756236 A	19971217
			WO 1998-EP8268 W	19981216

OTHER SOURCE(S): MARPAT 131:58849
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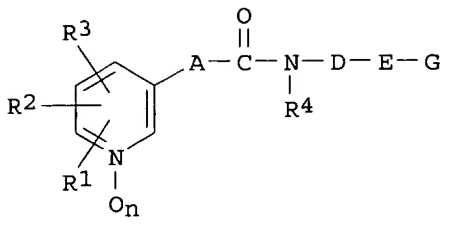

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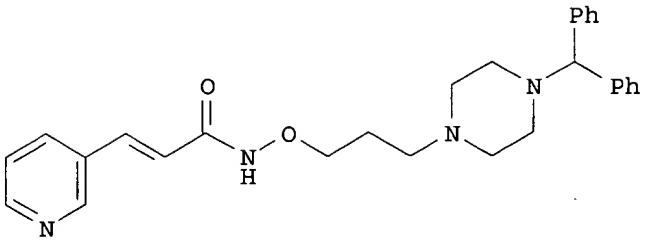


II

AB The invention relates to new piperazinyl-substituted pyridylalkanoic, -alkenoic, and alkynoic acid amides with a saturated or (poly)unsatd. hydrocarbon residue in the carboxylic acid group, and analogs, i.e., having formula I [R1 = H, OH, halo, cyano, CONH2, CO2H, (hetero)aryl, alkoxy, amino, (hetero)aryloxy, etc.; R2 = H, halo, cyano, alkyl, CF3, OH, etc.; or R1R2 = (CH2)4, (CH:CH)2, or CH2OCH2O or its (di)alkyl derivs.; R3 = H, halo, alkyl, CF3, hydroxyalkyl, etc.; R4 = H, OH, alk(en/yn)yl, cycloalkyl, alkoxy, aralkoxy; n = 0, 1; A = (un)substituted alkylene or hetero-isosteres, cycloalkylene, alkenylene, alkadienylene, or ethynylene; D = (un)substituted alkylene, alkenylene, alkynylene, or hetero-isosteres of them; E = (un)substituted (bis)(homo)piperazine bound at the N atoms; G = variety of terminal chains]. Also disclosed are methods for the production of the compds., medicaments containing them, and their production, as well as their therapeutic use, especially as cytostatic agents and immunosuppressive agents, for example, in the treatment or prevention of various types of tumors, and control of immune reactions such as autoimmune diseases. For example, 3-(3-pyridyl)acrylic acid was activated with oxalyl chloride and condensed with O-[3-[4-(diphenylmethyl)piperazin-1-yl]propyl]hydroxylamine to give title compound II. Several representative compds. inhibited various human tumor cells in vitro at low concns., e.g., with IC50 values of 0.1 nM to 10 μM, and also showed immunosuppressive activity against mouse lymphocytes with IC50 values of 0.03-0.09 μM.

IC ICM C07D213-56
ICS A61K031-495; C07F009-6509; C07D213-66; C07D401-12; C07D213-70; C07D213-64; C07D213-61; C07D487-08; C07D495-04; C07D405-12; C07D409-12; C07D491-04; C07D417-12; C07D513-04

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 15

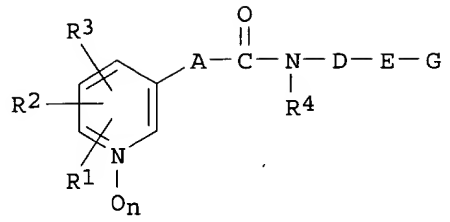
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:404929 CAPLUS
DOCUMENT NUMBER: 131:58756
TITLE: New piperidinyl-substituted pyridylalkane, -alkene, and -alkyne carboxamides, with antitumor and immunosuppressive activities

INVENTOR(S): **Biedermann, Elfi**; **Hasmann, Max**; **Loser, Roland**; Rattel, Benno; **Reiter, Friedemann**; Schein, Barbara; **Seibel, Klaus**; **Vogt, Klaus**; **Wosikowski, Katja**
PATENT ASSIGNEE(S): Klinge Pharma G.m.b.H., Germany
SOURCE: PCT Int. Appl., 217 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9931060	A2	19990624	WO 1998-EP8269		19981216
WO 9931060	A3	19990826			
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
DE 19756235	A1	19990701	DE 1997-19756235		19971217
ZA 9811241	A	19990609	ZA 1998-11241		19981208
AU 9921625	A1	19990705	AU 1999-21625		19981216
EP 1044197	A2	20001018	EP 1998-965846		19981216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2003525853	T2	20030902	JP 2000-538987		19981216
US 6593344	B1	20030715	US 2000-595547		20000616
PRIORITY APPLN. INFO.:			DE 1997-19756235	A	19971217
			WO 1998-EP8269	W	19981216

OTHER SOURCE(S): MARPAT 131:58756
GI



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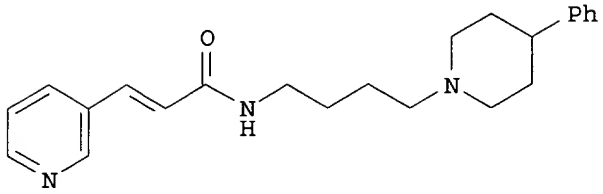

II

AB The invention relates to new piperidinyl-substituted pyridylalkanoic, -alkenoic, and alkynoic acid amides with a saturated or (poly)unsatd. hydrocarbon residue in the carboxylic acid group, and analogs, i.e., having formula I [R1 = H, OH, halo, cyano, CONH2, CO2H, (hetero)aryl, alkoxy, amino, (hetero)aryloxy, etc.; R2 = H, halo, cyano, alkyl, CF3, OH, etc.; or R1R2 = (CH2)4, (CH:CH)2, or CH2OCH2O or its (di)alkyl derivs.; R3 = H, halo, alkyl, CF3, hydroxyalkyl, etc.; R4 = H, OH, alk(en/yn)yl, cycloalkyl, alkoxy, aralkoxy; n = 0, 1; A = (un)substituted alkylene or hetero-isosteres, cycloalkylene, alkenylene, alkadienylene, hexatrienylene, or ethynylene; D = (un)substituted alkylene, alkenylene, alkynylene, or hetero-isosteres of them; E = (un)substituted piperidino or morpholino or their higher homologs, with an optional double bond; G = variety of terminal chains]. These substances have especially high cytostatic activities and pronounced immunosuppressive properties which make them suitable for therapeutic treatment in a broad spectrum of tumors. For example, 3-(3-pyridyl)acrylic acid was activated with oxalyl chloride in the presence of catalytic pyridine, and the resultant acid chloride was condensed with 4-(4-phenylpiperidin-1-yl)butylamine to give title compound II. Several representative compds. inhibited various human tumor cells in vitro at low concns., e.g., with IC50 values of 0.1 nM to 10 μM, and also showed immunosuppressive activity against mouse lymphocytes with IC50 values of, e.g., 0.5 μM.

IC ICM C07D213-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, CAPLUS, MEDLINE' - CONTINUE? (Y)/N:y

L215 ANSWER 7 OF 30 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005231662 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15867253
TITLE: Metabolic signatures associated with a NAD synthesis inhibitor-induced tumor apoptosis identified by

1H-decoupled-31P magnetic resonance spectroscopy.

AUTHOR: Muruganandham Manickam; Alfieri Alan A; Matei Cornelia; Chen Yuchun; Sukenick George; **Schemainda Isabel**; **Hasmann Max**; Saltz Leonard B; Koutcher Jason A
CORPORATE SOURCE: Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.

CONTRACT NUMBER: 1R24CA83084 (NCI)
P01 CA05826-038 (NCI)
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2005 May 1) 11 (9) 3503-13.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 20050504
Last Updated on STN: 20050802
Entered Medline: 20050801

ABSTRACT:
PURPOSE: Attempts to selectively initiate tumor cell death through inducible apoptotic pathways are increasingly being exploited as a potential anticancer strategy. Inhibition of NAD+ synthesis by a novel agent FK866 has been recently reported to induce apoptosis in human leukemia, hepatocarcinoma cells in vitro, and various types of tumor xenografts in vivo. In the present study, we used 1H-decoupled phosphorus (31P) magnetic resonance spectroscopy (MRS) to examine the metabolic changes associated with FK866 induced tumor cell death in a mouse mammary carcinoma. EXPERIMENTAL DESIGN: Induction of apoptosis in FK866-treated tumors was confirmed by histology and cytofluorometric analysis. FK866-induced changes in mammary carcinoma tumor metabolism in vivo were investigated using 1H-decoupled 31P MRS. To discern further the changes in metabolic profiles of tumors observed in vivo, high-resolution in vitro 1H-decoupled 31P MRS studies were carried out with perchloric acid extracts of mammary carcinoma tumors excised after similar treatments. In addition, the effects of FK866 on mammary carcinoma tumor growth and radiation sensitivity were studied. RESULTS: Treatment with FK866 induced a tumor growth delay and enhanced radiation sensitivity in mammary carcinoma tumors that was associated with significant increases in the 31P MR signal in the phosphomonoester region and a decrease in NAD+ levels, pH, and bioenergetic status. The 31P MRS of perchloric acid extracts of treated tumors identified the large unresolved signal in the phosphomonoester region as the resultant of resonances originating from intermediates of tumor glycolysis and guanylate synthesis in addition to alterations in pyridine nucleotide pools and phospholipid metabolism. CONCLUSION: The present results suggest that FK866 interferes with multiple biochemical pathways that contribute to the increased cell death (apoptosis) and subsequent radiation sensitivity observed in the mammary carcinoma that could be serially monitored by 31P MRS.

CONTROLLED TERM: Check Tags: Male
*Acrylamides: PD, pharmacology
Acrylamides: TU, therapeutic use
Animals
Annexin A5: ME, metabolism
*Apoptosis: DE, drug effects
Cell Cycle: DE, drug effects
Glycolysis: DE, drug effects
Guanine Nucleotides: ME, metabolism
Hydrogen-Ion Concentration: DE, drug effects
Intracellular Membranes: DE, drug effects
Intracellular Membranes: PH, physiology

*Magnetic Resonance Spectroscopy: MT, methods
Mammary Neoplasms, Experimental: ME, metabolism
Mammary Neoplasms, Experimental: PA, pathology
*Mammary Neoplasms, Experimental: PC, prevention & control
Membrane Potentials: DE, drug effects
Mice
Mice, Inbred C3H
Mitochondria: DE, drug effects
Mitochondria: PH, physiology
Mitosis: DE, drug effects
NAD: ME, metabolism
NADP: ME, metabolism
Neoplasm Transplantation
Pentosyltransferases: AI, antagonists & inhibitors
Phospholipids: ME, metabolism
*Piperidines: PD, pharmacology
Piperidines: TU, therapeutic use
Protein Binding: DE, drug effects
Research Support, N.I.H., Extramural
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Time Factors

CAS REGISTRY NO.: 53-59-8 (NADP); 53-84-9 (NAD)
CHEMICAL NAME: 0 (Acrylamides); 0 (Annexin A5); 0 (Guanine Nucleotides); 0 (N-(4-(1-benzoylpiperidin-4-yl)butyl)-3-(pyridin-3-yl)acrylamide); 0 (Phospholipids); 0 (Piperidines); EC 2.4.2. (Pentosyltransferases); EC 2.4.2.12 (nicotinamide phosphoribosyltransferase)

L215 ANSWER 8 OF 30 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003533377 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14612543
TITLE: FK866, a highly specific noncompetitive inhibitor of nicotinamide phosphoribosyltransferase, represents a novel mechanism for induction of tumor cell apoptosis.
AUTHOR: **Hasmann Max**; **Schemainda Isabel**
CORPORATE SOURCE: Fujisawa GmbH, Neumarkter Strasse 61, 81673 Munich, Germany.
SOURCE: Cancer research, (2003 Nov 1) 63 (21) 7436-42.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031113
Last Updated on STN: 20040117
Entered Medline: 20040116

ABSTRACT:
Deregulation of apoptosis, the physiological form of cell death, is closely associated with immunological diseases and cancer. Apoptosis is activated either by death receptor-driven or mitochondrial pathways, both of which may provide potential targets for novel anticancer drugs. Although several ligands stimulating death receptors have been described, the actual molecular events triggering the mitochondrial pathway are largely unknown. Here, we show initiation of apoptosis by gradual depletion of the intracellular coenzyme NAD+. We identified the first low molecular weight compound, designated FK866, which induces apoptosis by highly specific, noncompetitive inhibition of nicotinamide phosphoribosyltransferase (NAPRT), a key enzyme in the regulation of NAD+ biosynthesis from the natural precursor nicotinamide. Interference

with this enzyme does not primarily intoxicate cells because the mitochondrial respiratory activity and the NAD+ -dependent redox reactions involved remain unaffected as long as NAD+ is not effectively depleted by catabolic reactions. Certain tissues, however, have a high turnover of NAD+ through its cleavage by enzymes like poly(ADP-ribose) polymerase. Such cells often rely on the more readily available nicotinamide pathway for NAD+ synthesis and undergo apoptosis after inhibition of NAPRT, whereas cells effectively using the nicotinic acid pathway for NAD+ synthesis remain unaffected. In support of this concept, FK866 effectively induced delayed cell death by apoptosis in HepG2 human liver carcinoma cells with an IC(50) of approximately 1 nM, did not directly inhibit mitochondrial respiratory activity, but caused gradual NAD+ depletion through specific inhibition of NAPRT. This enzyme, when partially purified from K562 human leukemia cells, was noncompetitively inhibited by FK866, and the inhibitor constants were calculated to be 0.4 nM for the enzyme/substrate complex (K(i)) and 0.3 nM for the free enzyme (K(i)'), respectively. Nicotinic acid and nicotinamide were both found to have antidote potential for the cellular effects of FK866. FK866 may be used for treatment of diseases implicating deregulated apoptosis such as cancer for immunosuppression or as a sensitizer for genotoxic agents. Furthermore, it may provide an important tool for investigation of the molecular triggers of the mitochondrial pathway leading to apoptosis through enabling temporal separation of NAD+ decrease from ATP breakdown and apoptosis by several days

CONTROLLED TERM:
*Acrylamides: PD, pharmacology
Adenosine Triphosphate: ME, metabolism
*Antineoplastic Agents: PD, pharmacology
*Apoptosis: DE, drug effects
Carcinoma, Hepatocellular: DT, drug therapy
Carcinoma, Hepatocellular: EN, enzymology
Carcinoma, Hepatocellular: PA, pathology
Cell Line, Tumor
*Enzyme Inhibitors: PD, pharmacology
Humans
K562 Cells
Kinetics
Liver Neoplasms: DT, drug therapy
Liver Neoplasms: EN, enzymology
Liver Neoplasms: PA, pathology
Mitochondria, Liver: DE, drug effects
Mitochondria, Liver: ME, metabolism
NAD: ME, metabolism
Niacin: PD, pharmacology
Niacinamide: PD, pharmacology
Oxygen Consumption: DE, drug effects
*Pentosyltransferases: AI, antagonists & inhibitors
*Piperidines: PD, pharmacology

CAS REGISTRY NO.: 53-84-9 (NAD); 56-65-5 (Adenosine Triphosphate); 59-67-6 (Niacin); 98-92-0 (Niacinamide)

CHEMICAL NAME: 0 (Acrylamides); 0 (Antineoplastic Agents); 0 (Enzyme Inhibitors); 0 (N-(4-(1-benzoylpiperidin-4-yl)butyl)-3-(pyridin-3-yl)acrylamide); 0 (Piperidines); EC 2.4.2. (Pentosyltransferases); EC 2.4.2.12 (nicotinamide phosphoribosyltransferase)

L215 ANSWER 9 OF 30 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004092846 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14981935
TITLE: Antiangiogenic potency of FK866/K22.175, a new inhibitor of intracellular NAD biosynthesis, in murine renal cell carcinoma.
AUTHOR: Drevs Joachim; **Loser Roland**; **Rattel Benno**

; Esser Norbert
CORPORATE SOURCE: Department of Medical Oncology, Tumor Biology Center, Breisacher Strasse 117, D-79106 Freiburg, Federal Republic of Germany.. drevs@tumorbio.uni-freiburg.de
SOURCE: Anticancer research, (2003 Nov-Dec) 23 (6C) 4853-8.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20040402
Entered Medline: 20040401

ABSTRACT:
FK866/K22.175 (FK-866), developed as an anticancer agent, interferes with the NAD+ biosynthesis and therefore might have characteristics distinct from conventional chemotherapeutic agents. We investigated FK-866 in a murine renal cell carcinoma model (RENCA) to assess its antitumor, antimetastatic and antiangiogenic potency. FK-866 was administered twice daily on days 10 to 15 after intrarenal inoculation of RENCA cells in syngenic Balb/c mice at oral doses of 6, 10, 14 and 18 mg/kg to define the optimal dose related to toxicity. For efficacy studies, FK-866 was administered orally twice daily at doses of 6 and 10 mg/kg or twice daily at doses of 3 and 5 mg/kg on days 14 to 19 after tumor cell inoculation. Animals in the positive control group received 30 mg/kg TNP 470 subcutaneously on every other day beginning on day 1. On day 17, all animals were examined for blood flow in the left renal artery by color Doppler imaging (CDI). The animals were sacrificed on day 21 and analyzed for primary tumor weight and volume, number of metastases to the lung and abdominal lymph nodes and vessel density in tumor tissues. Doses of up to 6 mg/kg FK-866 were less toxic than treatment with TNP-470. Significant antitumor efficacy was observed for doses of > or = 10 mg/kg FK-866 only. In contrast, a significant decrease of vessel density in tumor tissues by up to 70% could be detected for all dose groups. Changes in blood flow in the tumor feeding renal artery could not be detected because of the profound strong tumor reduction. FK-866 has antitumoral and antimetastatic activity in RENCA mice. Furthermore, this is the first report to describe a strong antiangiogenic potency of FK-866.

CONTROLLED TERM:
*Acrylamides: PD, pharmacology
Acrylamides: TO, toxicity
*Angiogenesis Inhibitors: PD, pharmacology
Angiogenesis Inhibitors: TO, toxicity
Animals
*Antineoplastic Agents: PD, pharmacology
Antineoplastic Agents: TO, toxicity
*Blood Flow Velocity: DE, drug effects
Body Weight: DE, drug effects
*Carcinoma, Renal Cell: BS, blood supply
*Carcinoma, Renal Cell: DT, drug therapy
Carcinoma, Renal Cell: PA, pathology
Carcinoma, Renal Cell: US, ultrasonography
*Kidney Neoplasms: BS, blood supply
*Kidney Neoplasms: DT, drug therapy
Kidney Neoplasms: PA, pathology
Kidney Neoplasms: US, ultrasonography
Mice
*NAD: BI, biosynthesis
Neovascularization, Pathologic: PC, prevention & control
*Piperidines: PD, pharmacology
Piperidines: TO, toxicity
Tumor Cells, Cultured

CAS REGISTRY NO.: 53-84-9 (NAD)
CHEMICAL NAME: 0 (Acrylamides); 0 (Angiogenesis Inhibitors); 0 (Antineoplastic Agents); 0 (N-(4-(1-benzoylpiperidin-4-yl)butyl)-3-(pyridin-3-yl)acrylamide); 0 (Piperidines)

L215 ANSWER 10 OF 30 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003217176 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12738750
TITLE: In vitro and in vivo antitumor activity of methotrexate conjugated to human serum albumin in human cancer cells.
AUTHOR: **Wosikowski Katja**; **Biedermann Elfi**; **Rattel Benno**; Breiter Norbert; Jank Peter; **Loser Roland**; Jansen Gerrit; Peters Godefridus J
CORPORATE SOURCE: Pharmacology Department, Fujisawa-Deutschland, 81673 Munich, Germany.
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2003 May) 9 (5) 1917-26.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030513
Last Updated on STN: 20040113
Entered Medline: 20040112

ABSTRACT:
To avoid systemic toxicity of the cytotoxic drug methotrexate (MTX) and to improve tumor selectivity, MTX was bound to human serum albumin (HSA) as a drug carrier. To understand more about the mechanism of action of MTX conjugated to HSA (MTX-HSA), the uptake of MTX-HSA into the cell was determined as well as the effect of MTX-HSA on thymidylate synthase (TS), cell cycle distribution, and cell proliferation. Different uptake kinetics were observed for [(3)H]MTX and [(3)H]MTX-HSA. However, similar uptake kinetics were measured for (125)I-HSA and (125)I-MTX-HSA (2.1 and 1.8 pmol/10(7) cells/h when cells were treated with 10 micro M (125)I-HSA and (125)I-MTX-HSA, respectively), suggesting that MTX-HSA enters the cells by albumin-mediated endocytosis. We observed no effect of MTX-HSA on TS when folate receptor-expressing KB cells were treated for 4 h (IC(50), >50 micro M). However, 24 h after incubation, MTX-HSA inhibited TS with an IC(50) of 6.9 micro M. In addition, we found that MTX-HSA had a delayed effect on the cell cycle compared with MTX and that this effect could be inhibited with the lysosomal inhibitor methylamine, suggesting that MTX-HSA activity is dependent on lysosomal processes. The proliferation of different wild-type and MTX-resistant tumor cell lines was inhibited at IC(50) concentrations between 2 and 78 micro M, respectively. MTX-HSA accumulates in vivo in the tumor tissue. Local concentrations of 18-29 micro M were measured, which are effective antiproliferative concentrations as determined in vitro. We also investigated the antitumor activity of MTX-HSA in vivo in different human tumor xenografts grown s.c. in nude mice. Fourteen tumors from eight different tissues were tested. Nine of 14 tumors (64%) showed a clear response with tumor inhibition, stasis, or regression; 5 of 14 (36%) gave a moderate response with tumor growth delay or no response. In conclusion, MTX-HSA is effectively taken up by the cells via albumin receptor- or folate receptor-mediated endocytosis and time-dependently released as an active compound into the cytosol to exert an inhibiting effect on TS and to induce cell cycle alterations. In vivo, effective concentrations of MTX-HSA were reached in tumor tissue to exhibit antitumor activity.
CONTROLLED TERM: Check Tags: In Vitro; Male Animals

*Antineoplastic Agents: TU, therapeutic use
Cell Cycle: DE, drug effects
Cell Division: DE, drug effects
Humans
*Methotrexate: TU, therapeutic use
Mice
Mice, Nude
Neoplasm Transplantation
*Neoplasms: DT, drug therapy
Neoplasms: PA, pathology
Research Support, Non-U.S. Gov't
Serum Albumin: AE, adverse effects
*Serum Albumin: TU, therapeutic use
Thymidylate Synthase: AI, antagonists & inhibitors
Thymidylate Synthase: ME, metabolism
Transplantation, Heterologous
Tumor Cells, Cultured

CAS REGISTRY NO.: 59-05-2 (Methotrexate)
CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Serum Albumin); 0 (methotrexate-serum albumin); EC 2.1.1.45 (Thymidylate Synthase)

L215 ANSWER 11 OF 30 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002125775 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11861382
TITLE: WK175, a novel antitumor agent, decreases the intracellular nicotinamide adenine dinucleotide concentration and induces the apoptotic cascade in human leukemia cells.
AUTHOR: **Wosikowski Katja**; Mattern Karin; **Schemainda Isabel**; **Hasmann Max**; **Rattel Benno**; **Loser Roland**
CORPORATE SOURCE: Pharmacology Department, Klinge Pharma, 81673 Munich, Germany.. katja.wosikowski@wilex.de
SOURCE: Cancer research, (2002 Feb 15) 62 (4) 1057-62. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020226
Last Updated on STN: 20020403
Entered Medline: 20020327

ABSTRACT:
We recently developed a class of novel antitumor agents that elicit a potent growth-inhibitory response in many tumor cells cultured in vitro. WK175, a member of this class, was chosen as a model compound that showed strong in vitro efficacy. WK175 interferes with the intracellular steady-state level of NAD(+), resulting in a decreased cellular NAD(+) concentration. We found that WK175 induces apoptotic cell death without any DNA-damaging effect. The apoptotic death signaling pathway initiated by WK175 was examined in detail: mitochondrial membrane potential, cytochrome c release, caspase 3 activation, caspase 3 and poly(ADP-ribose) polymerase cleavage, and the appearance of a sub-G(1) cell cycle population were determined in time course studies in THP-1 (a human monocytic leukemia cell line) cells. We found activation of this cascade after 24 h of treatment with 10 nM WK175. Induction of apoptosis was prevented by bongkrekic acid, Z-Asp-Glu-Val-Asp-fluoromethylketone, and Z-Leu-Glu-His-Asp-fluoromethylketone, inhibitors of the mitochondrial permeability transition and of caspase 3 and 9, respectively, but not by Ac-Tyr-Val-Ala-Asp-CHO, a specific caspase 1 inhibitor, suggesting the

involvement of the permeability transition pore, caspase 3, and caspase 9 in the WK175-induced apoptotic cascade. These results imply that decreased NAD(+) concentration initiates the apoptotic cascade, resulting in the antitumor effect of WK175.

CONTROLLED TERM: Antineoplastic Agents: AI, antagonists & inhibitors
*Antineoplastic Agents: PD, pharmacology
*Apoptosis: DE, drug effects
Apoptosis: PH, physiology
Bongkrekic Acid: PD, pharmacology
Caspases: AI, antagonists & inhibitors
Caspases: ME, metabolism
Cell Cycle: DE, drug effects
Cell Cycle: PH, physiology
Cytochrome c Group: ME, metabolism
Cytochrome c Group: SE, secretion
DNA, Neoplasm: ME, metabolism
Enzyme Activation
Enzyme Inhibitors: PD, pharmacology
Humans
Intracellular Membranes: DE, drug effects
Intracellular Membranes: PH, physiology
Leukemia, Monocytic, Acute: DT, drug therapy
*Leukemia, Monocytic, Acute: ME, metabolism
*Leukemia, Monocytic, Acute: PA, pathology
Membrane Potentials: DE, drug effects
Mitochondria: DE, drug effects
Mitochondria: PH, physiology
*NAD: ME, metabolism
*Organic Chemicals
Poly(ADP-ribose) Polymerases: ME, metabolism
Subcellular Fractions: ME, metabolism
Tumor Cells, Cultured

CAS REGISTRY NO.: 11076-19-0 (Bongkrekic Acid); 53-84-9 (NAD)

CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Cytochrome c Group); 0 (DNA, Neoplasm); 0 (Enzyme Inhibitors); 0 (Organic Chemicals); 0 (WK175); EC 2.4.2.30 (Poly(ADP-ribose) Polymerases); EC 3.4.22.- (Caspases); EC 3.4.22.- (caspase 9); EC 3.4.22.- (caspase-3)

L215 ANSWER 12 OF 30 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2002705555 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12467305

TITLE: Cytoprotective features of selenazofurin in hematopoietic cells.

AUTHOR: Pogrebniak A; **Hasmann M**; **Schemainda I**; Pelka-Fleischer R; Nuessler V

CORPORATE SOURCE: Medizinische Klinik III, Forschungslabor A, Klinikum Grosshadem, Munich, Germany.

SOURCE: International journal of clinical pharmacology and therapeutics, (2002 Aug) 40 (8) 368-75. Journal code: 9423309. ISSN: 0946-1965.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200402

ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20021217
Entered Medline: 20040204

ABSTRACT:

OBJECTIVES: Antineoplastic activity of tiazofurin (Tz) and selenazofurin (Se) depends on their conversion to substances which are analogs of NAD. NAD performs pleiotropic and essential cellular functions, both as a cofactor in oxidation-reduction reactions and as a substrate for poly- and mono-ADP-ribosylation reactions. The therapeutic potential of modulating intracellular NAD levels and activity of NAD-dependent enzymes by concomitant administration of conventional anticancer agents merits further research. Our aim was to investigate the cytotoxic effects of Tz and Se in hematopoietic cells and to test their ability to potentiate the effects of DNA strand-disrupting agents. MATERIAL: THP-1, a cell line, derived from human acute monoblastic leukemia, was used. CLL lymphocytes were obtained from 8 patients with CLL. METHODS: The WST-1 test was used to detect the function of NAD(P)-dependent dehydrogenases after exposure of THP-1 cells to Tz or Se. Cytotoxicity of Tz, Se, MNNG and chlorambucil was assessed using the membrane permeability assay (PI test). RESULTS: THP-1 cells were sensitive to cytotoxic effects of Tz and Se, with IC50 values of 2.5 x 10(-5) M for Tz and 2 x 10(-6) M for Se, as determined with the WST-1 test; 10 microM Se induced cell membrane disruption in more than 20% of THP-1 cells 48 hours after commencement of treatment, whereas the same concentration of Tz failed to increase membrane permeability. Pretreatment of THP-1 cells with 0.5 - 1.5 microM Se had no effect on the time course of cell death, induced by treatment with the DNA-damaging agent 1-methyl-3-nitro-1 - nitrosoguanidinium (MNNG) for 36 hours. However, when incubation of THP-1 cells with MNNG was prolonged (72 hours) without changing the incubation medium, pretreatment with Se had the following effects: the relative number of cells that died spontaneously decreased, and the cytotoxicity of MNNG was diminished. This effect was also demonstrated ex vivo in 6 of 8 cases of CLL, treated with MNNG and chlorambucil. CONCLUSIONS: Contrary to other investigations, we here demonstrate that preincubation with Se may partially protect cells from cell death induced by the alkylating agents MNNG and chlorambucil in the THP-1 cell line and in CLL lymphocytes presumably by affecting spontaneous cell death.

CONTROLLED TERM:
Antineoplastic Agents: ME, metabolism
*Antineoplastic Agents: PD, pharmacology
*Antineoplastic Agents: TU, therapeutic use
Cell Death: DE, drug effects
Cell Line
Cell Survival: DE, drug effects
Chlorambucil: PD, pharmacology
Dose-Response Relationship, Drug
Humans
Leukemia, Lymphocytic, Chronic: DT, drug therapy
Leukemia, Monocytic, Acute: DT, drug therapy
Methylnitronitrosoguanidine: PD, pharmacology
Organoselenium Compounds: ME, metabolism
*Organoselenium Compounds: PD, pharmacology
*Organoselenium Compounds: TU, therapeutic use
*Ribavirin: AA, analogs & derivatives
Ribavirin: ME, metabolism
Ribavirin: PD, pharmacology
Ribavirin: TU, therapeutic use
Ribonucleosides: ME, metabolism
*Ribonucleosides: PD, pharmacology
*Ribonucleosides: TU, therapeutic use

CAS REGISTRY NO.: 305-03-3 (Chlorambucil); 36791-04-5 (Ribavirin); 60084-10-8 (tiazofurin); 70-25-7 (Methylnitronitrosoguanidine); 83705-13-9 (selenazofurin)

CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Organoselenium Compounds); 0 (Ribonucleosides)

L215 ANSWER 13 OF 30 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 1999119023 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9922050
TITLE: In vitro efficacy of known P-glycoprotein modulators compared to droloxifene E and Z: studies on a human T-cell leukemia cell line and their resistant variants.
AUTHOR: Nussler V; Pelka-Fleisc R; Gieseler F; **Hasmann M**; **Loser R**; Gullis E; Stotzer O; Zwierzina H; Wilmanns W
CORPORATE SOURCE: Med. Klinik III, Klinikum Grosshadern, Munich, Germany.. nuessler@gsf.de
SOURCE: Leukemia & lymphoma, (1998 Nov) 31 (5-6) 589-97.
Journal code: 9007422. ISSN: 1042-8194.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990513

ABSTRACT:
P-glycoprotein(P-gp)- related resistance is one of the major obstacles in treating leukemia patients. Therefore, it is of clinical interest to find new potential modulators and compare their P-gp-modulating efficacy. The present analysis investigated the influence of P-gp modulators, such as verapamil, tamoxifen, droloxifene E, droloxifene Z, SDZ PSC 833 (PSC 833) and dexniguldipine in a leukemic T-cell line (CCRF-CEM) and its P-gp-resistant counterparts (CCRF-CEM/ACT400 and CCRF-CEM/VCR1000). P-gp expression was assessed with an immunocytological technique using the monoclonal antibody 4E3.16. It was characterized as the percentage of P-gp positive cells and also expressed as a D value by using the Kolmogorov Smirnov statistic. The efficacy of P-gp modulators was determined with the rhodamine-123 accumulation test and the MTT test. An in vitro modulator concentration between 0.1 microM and 3 microM was determined, where no genuine antiproliferative effect was apparent. The modulators PSC 833 and dexniguldipine were the significant ($p<C0.05$) most potent chemosensitizers followed by verapamil, droloxifene Z, tamoxifen and droloxifene E in descending order. In addition to the modulators PSC 833 and dexniguldipine, droloxifene Z should especially be considered as a candidate for future ex vivo and in vivo studies. The main advantage of droloxifene Z could be the low rate of expected side effects. This fact permits the use of high Drol Z dosage in order to achieve a relevant modulating effect in vivo and to use this drug in combination with a further modulator so as to reach maximum efficacy with tolerable side effects.

CONTROLLED TERM: Check Tags: Comparative Study
ATP-Binding Cassette Transporters: AN, analysis
Antibodies, Monoclonal: IM, immunology
Cell Division: DE, drug effects
*Cyclosporins: PD, pharmacology
*Dihydropyridines: PD, pharmacology
*Drug Resistance, Multiple
*Drug Resistance, Neoplasm
Drug Screening Assays, Antitumor
Humans
*Leukemia, T-Cell: PA, pathology
Multidrug Resistance-Associated Proteins
*Neoplasm Proteins: AI, antagonists & inhibitors
*P-Glycoprotein: AI, antagonists & inhibitors
*Tamoxifen: AA, analogs & derivatives
*Tamoxifen: PD, pharmacology
Tumor Cells, Cultured: DE, drug effects

Vault Ribonucleoprotein Particles
*Verapamil: PD, pharmacology
CAS REGISTRY NO.: 102993-22-6 (niguldipine); 10540-29-1 (Tamoxifen); 121584-18-7 (valspodar); 52-53-9 (Verapamil); 82413-20-5 (3-hydroxytamoxifen)
CHEMICAL NAME: 0 (ATP-Binding Cassette Transporters); 0 (Antibodies, Monoclonal); 0 (Cyclosporins); 0 (Dihydropyridines); 0 (Multidrug Resistance-Associated Proteins); 0 (Neoplasm Proteins); 0 (P-Glycoprotein); 0 (Vault Ribonucleoprotein Particles); 0 (lung resistance protein)

L215 ANSWER 14 OF 30 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 95291560 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7773504
TITLE: Intracellular localization, vesicular accumulation and kinetics of daunorubicin in sensitive and multidrug-resistant gastric carcinoma EPG85-257 cells.
AUTHOR: Seidel A; **Hasmann M**; **Loser R**; Bunge A; Schaefer B; Herzig I; Steidtmann K; Dietel M
CORPORATE SOURCE: Institute of Pathology/Charite, Humboldt-Universitat zu Berlin, Germany.
SOURCE: Virchows Archiv : an international journal of pathology, (1995) 426 (3) 249-56.
Journal code: 9423843. ISSN: 0945-6317.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950720
Last Updated on STN: 19970203
Entered Medline: 19950712

ABSTRACT:
In the human gastric carcinoma cell line EPG85-257P (parent) induction of resistance to daunorubicin (DAU) was achieved by selection with stepwise increased concentrations of the drug. The new variant was named EPG85-257DAU and was shown to overexpress the mdr1 gene product 170 kDa P-glycoprotein (P-Gp) as demonstrated by immunocytochemistry and mdr1-specific RT-PCR. To investigate the intracellular pathway of DAU the subcellular distribution of this autofluorescent drug was studied in the resistant cells and compared to its chemosensitive counterpart EPG85-257P. When sensitive cells were exposed to DAU the drug rapidly accumulated in the nucleus until cell death. No redistribution of DAU to the cytoplasm was observed. In resistant cells exposed to the drug DAU also accumulated in the nucleus but to a lesser extent than in parent cells. Following exposure, nuclear fluorescence was observed to decrease over a time period of up to 48 h. Six hours after DAU exposure formation of fluorescent vesicle formation started in the perinuclear region and increased continuously. After 48 h nuclear fluorescence was no longer detectable and DAU was located exclusively in vesicles. During this period the vesicles moved from the region of origin to the cell periphery. A pulse chase experiment showed, that vesicles may contain DAU derived from the nucleus. Treatment of EPG85-257DAU cells with DAU in conjunction with the chemosensitizer cyclosporin A (CsA) increased nuclear fluorescence without impairing vesicle formation. Disruption of microtubules by nocodazole led to an accumulation of vesicles in the perinuclear region indicating that microtubules are involved in vesicular transport. Treatment of EPG85-257DAU cells with the actin disruptor cytochalasin B led to accumulation of vesicles in the cell periphery indicating that actin may be involved in exocytosis. Uptake and efflux of DAU and rhodamin (RH) were determined in sensitive and resistant cells using a fluorescence activated cell sorter. Uptake of both

compounds was distinctly lower in resistant than in sensitive cells. When resistant cells preloaded for 2 h with RH subsequently were incubated in drug free medium the substance was rapidly released indicating transmembrane transport by P-Gp. In contrast, despite expression of P-Gp in resistant cells no considerable release of DAU was observed for up to 2 h under the same experimental protocol. This indicates that in resistant cells intracellular DAU at least in part may be inaccessible for P-Gp and that vesicular drug transport appears to contribute to DAU resistance by removing intracellular DAU via exocytosis.

CONTROLLED TERM: Cyclosporine: PD, pharmacology
Cytochalasin B: PD, pharmacology
*Daunorubicin: AN, analysis
*Daunorubicin: ME, metabolism
*Drug Resistance, Multiple: PH, physiology
Flow Cytometry
Humans
Nocodazole: PD, pharmacology
P-Glycoprotein: BI, biosynthesis
Polymerase Chain Reaction
RNA, Messenger: BI, biosynthesis
*Stomach Neoplasms: CH, chemistry
Stomach Neoplasms: PA, pathology
*Stomach Neoplasms: UL, ultrastructure
Tumor Cells, Cultured

CAS REGISTRY NO.: 14930-96-2 (Cytochalasin B); 20830-81-3 (Daunorubicin); 31430-18-9 (Nocodazole); 59865-13-3 (Cyclosporine)

CHEMICAL NAME: 0 (P-Glycoprotein); 0 (RNA, Messenger)

L215 ANSWER 15 OF 30 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 94356885 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8076367

TITLE: Preclinical data for Droloxifene.

AUTHOR: **Hasmann M; Rattel B; Loser R**

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Klinge Pharma GmbH, Munich, Germany.

SOURCE: Cancer letters, (1994 Sep 15) 84 (2) 101-16. Ref: 43
Journal code: 7600053. ISSN: 0304-3835.

PUB. COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199410

ENTRY DATE: Entered STN: 19941013
Last Updated on STN: 19960129
Entered Medline: 19941004

ABSTRACT:
The new antiestrogen Droloxifene has a 10-60-fold higher binding affinity to the estrogen receptor (ER) compared to the related compound Tamoxifen. A similar relationship was found in growth inhibition studies which showed that Droloxifene inhibited the different ER positive human breast cancer cells more effectively than Tamoxifen, predominantly in drug concentrations which are found in humans during therapy. As another consequence of the high stability of the complex formed by Droloxifene binding to the ER, intermittent exposures with clinically relevant concentrations of Droloxifene brought about effective growth inhibition of human ER positive tumor cells even after short-term application. Droloxifene was found, like Tamoxifen, to block human breast cancer cells in G1-phase of the cell cycle. Moreover, cell-cycle data confirmed the superior growth-inhibiting potency of Droloxifene compared to Tamoxifen. Droloxifene was also found to effectively induce expression of the

negative growth factor TGF-beta, to inhibit IGF-I stimulated cell growth and to prevent estrogen-stimulated proto-oncogene c-myc expression. Unlike Tamoxifen, Droloxifene is a potent inhibitor of protein biosynthesis in ER-positive breast cancer cells at physiologically relevant concentrations. Lower estrogenic and higher antiestrogenic effects on immature rat uterus indicate a higher therapeutic index for Droloxifene compared to Tamoxifen. In vivo, Droloxifene displayed increased growth inhibition of different tumors of animal (R3230AC and 13762) and human origin (T61). Furthermore, it was found that the two structurally similar drugs differ in their toxicologic characteristics in the following important respects: Droloxifene is devoid of any in vivo or in vitro carcinogenic or mutagenic effects, whereas Tamoxifen causes liver tumors in rats, induces DNA adduct formation in rats and hamsters and shows transforming activity in SHE-cells (Syrian hamster embryo fibroblasts). Considerably less toxicity and a lower level of intrinsic estrogenicity was observed even after maximum long-term exposure of different animal species to Droloxifene, in comparison with Tamoxifen. Therefore, it can be assumed that Droloxifene may represent an important step forward in the treatment of mammary carcinomas in women through its better tolerability and increased efficacy compared with Tamoxifen. For long-term adjuvant or preventive treatment of breast cancer, Droloxifene may well be the safer choice.

CONTROLLED TERM: Check Tags: Female
Animals
*Antineoplastic Agents: TU, therapeutic use
Breast Neoplasms: DT, drug therapy
Cell Cycle
Drug Evaluation, Preclinical
*Estrogen Antagonists: TU, therapeutic use
Humans
Insulin-Like Growth Factor I: PD, pharmacology
Rats
Rats, Inbred Strains
Receptors, Estrogen: ME, metabolism
*Tamoxifen: AA, analogs & derivatives
Tamoxifen: PD, pharmacology
Tamoxifen: TU, therapeutic use
Transforming Growth Factor beta: ME, metabolism

CAS REGISTRY NO.: 10540-29-1 (Tamoxifen); 67763-96-6 (Insulin-Like Growth Factor I); 82413-20-5 (3-hydroxytamoxifen)

CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Estrogen Antagonists); 0 (Receptors, Estrogen); 0 (Transforming Growth Factor beta)

L215 ANSWER 16 OF 30 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 93146651 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8425767

TITLE: Inhibition of growth-factor-activated proliferation by anti-estrogens and effects on early gene expression of MCF-7 cells.

AUTHOR: **Wosikowski K**; Kung W; **Hasmann M**; **Loser R**; Eppenberger U

CORPORATE SOURCE: Department of Research, Kantonsspital Basel, Switzerland.

SOURCE: International journal of cancer. Journal international du cancer, (1993 Jan 21) 53 (2) 290-7.
Journal code: 0042124. ISSN: 0020-7136.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199303

ENTRY DATE: Entered STN: 19930312
Last Updated on STN: 20000303

Entered Medline: 19930304

ABSTRACT:
Recently, it was reported that the anti-estrogen tamoxifen not only inhibits estradiol-stimulated growth of MCF-7 cells but also significantly reduces the proliferation rate of cells stimulated by growth factors. We have confirmed this finding and also shown that the new anti-estrogen droloxifene inhibits the proliferation of epidermal growth factor (EGF) and insulin-like growth factor-I (IGF-I)-stimulated MCF-7 cells. The growth-factor-induced proliferation was inhibited in a dose-dependent manner by the anti-estrogens in the complete absence of estrogen and FCS. Of the anti-estrogens, droloxifene was considerably more potent than tamoxifen. Because the expression of the proto-oncogenes c-fos and c-myc has been considered a key event in development of the mitogenic response, we examined the effects of anti-estrogens on c-myc and c-fos gene expression. We included in these investigations the steroidal anti-estrogen ICI 164,384 because this compound has no or very little estrogenic activity. The studies revealed that all 3 anti-estrogens transiently induced c-myc mRNA expression. However, the anti-estrogens inhibited estradiol-induced c-myc mRNA expression, although with different potencies. Pre-incubation of MCF-7 cells with droloxifene and tamoxifen resulted in elevated levels of growth-factor-induced c-myc mRNA expression. In contrast, the anti-estrogens did not induce c-fos mRNA or affect the expression of c-fos mRNA induced by growth factors. In conclusion, non-steroidal anti-estrogens inhibit growth-factor-stimulated proliferation of MCF-7 cells without inhibiting growth-factor-induced c-myc or c-fos mRNA expression.

CONTROLLED TERM:
Breast Neoplasms: GE, genetics
*Breast Neoplasms: PA, pathology
Cell Division: DE, drug effects
*Epidermal Growth Factor: AI, antagonists & inhibitors
Estradiol: PD, pharmacology
*Estrogen Antagonists: PD, pharmacology
*Gene Expression Regulation, Neoplastic: DE, drug effects
Genes, fos: DE, drug effects
Genes, myc: DE, drug effects
Humans
*Insulin-Like Growth Factor I: AI, antagonists & inhibitors
RNA, Messenger: DE, drug effects
RNA, Neoplasm: DE, drug effects
Research Support, Non-U.S. Gov't
Signal Transduction: DE, drug effects
Tumor Cells, Cultured

CAS REGISTRY NO.: 50-28-2 (Estradiol); 62229-50-9 (Epidermal Growth Factor); 67763-96-6 (Insulin-Like Growth Factor I)

CHEMICAL NAME: 0 (Estrogen Antagonists); 0 (RNA, Messenger); 0 (RNA, Neoplasm)

GENE NAME: c-fos; c-myc

L215 ANSWER 17 OF 30 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER: 90216971 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1691199

TITLE: Flow cytometric analysis of virus-infected cells and its potential use for screening antiviral agents.

AUTHOR: Steele-Mortimer O A; Meier-Ewert H; **Loser R**; **Hasmann M J**

CORPORATE SOURCE: Abteilung fur Virologie, Technischen Universitat Munchen, F.R.G.

SOURCE: Journal of virological methods, (1990 Mar) 27 (3) 241-52. Journal code: 8005839. ISSN: 0166-0934.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900622
Last Updated on STN: 19970203
Entered Medline: 19900524

ABSTRACT:
Virus-infected cells were analyzed using multiparameter flow cytometry. Two virus-cell systems were investigated: HSV-1-infected VF cells and influenza C virus JHB/1/66-infected MDCK cells. Analysis included the measurement of the appearance of virus specific antigens. On individual cells, with polyclonal antibodies, antigens were first detected at 12 h p.i., and the numbers of labeled cells were followed up to 96 h p.i. The efficacy of four antiviral agents was tested with this system. The results were in good agreement with those of plaque reduction tests and indicated that this new method may be extremely useful for the correlation of viral and cellular events with antiviral activity. Finally, it was demonstrated that infected cells in both systems have a considerably greater volume than non-infected cells.

CONTROLLED TERM: Check Tags: Comparative Study
Animals
Antigens, Viral: BI, biosynthesis
*Antiviral Agents
Cell Survival
Cells, Cultured
*Drug Evaluation, Preclinical: MT, methods
Evaluation Studies
*Flow Cytometry
Fluorescein-5-isothiocyanate
Fluoresceins
Fluorescent Antibody Technique
Humans
Influenzavirus C: DE, drug effects
Influenzavirus C: IM, immunology
Plaque Assay
Simplexvirus: DE, drug effects
Simplexvirus: IM, immunology
Staining and Labeling
Thiocyanates
Time Factors

CAS REGISTRY NO.: 3326-32-7 (Fluorescein-5-isothiocyanate)
CHEMICAL NAME: 0 (Antigens, Viral); 0 (Antiviral Agents); 0 (Fluoresceins); 0 (Thiocyanates)

L215 ANSWER 18 OF 30 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 91197199 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2085283
TITLE: The hypolipidemic effect of lifibrol during a long term treatment of pigs.
AUTHOR: Schliack M; **Loser R**; **Seibel K**; **Rattel B**; Lang G
CORPORATE SOURCE: Klinge Pharma GmbH, Munchen, F.R.G.
SOURCE: Artery, (1990) 18 (1) 1-15.
Journal code: 7508494. ISSN: 0098-6127.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910602
Last Updated on STN: 19980206
Entered Medline: 19910516

ABSTRACT:
We investigated the hypolipidemic property of lifibrol in male and female minipigs in a long term trial over a treatment period of 6 months. Oral dosages between 12.5 mg/kg BW and 100 mg/kg BW lifibrol resulted in a strong reduction of serum cholesterol after only two weeks of treatment. The hypocholesterolemic effect was not counterbalanced and reached -76% at the end of the trial in the male pigs and -70% in the female pigs (100 mg/kg BW lifibrol). The reduction of serum cholesterol was mainly brought about by the reduction of LDL-cholesterol. Serum triglycerides seemed to be less influenced by lifibrol than serum cholesterol. The application of lifibrol had no significant influence on the weight gain of the pigs and did not alter the serum levels of AST and ALT. Lifibrol was well tolerated and the animals showed no symptoms of incompatibility.

CONTROLLED TERM: Check Tags: Female; Male
Alanine Transaminase: BL, blood
Animals
*Anticholesteremic Agents
*Antilipemic Agents: PD, pharmacology
Aspartate Aminotransferases: BL, blood
Body Weight: DE, drug effects
*Butanols: PD, pharmacology
Cholesterol: BL, blood
*Hydroxybenzoic Acids: PD, pharmacology
Sex Factors
Swine
Swine, Miniature
Time Factors
Triglycerides: BL, blood

CAS REGISTRY NO.: 57-88-5 (Cholesterol); 96609-16-4 (lifibrol)

CHEMICAL NAME: 0 (Anticholesteremic Agents); 0 (Antilipemic Agents); 0 (Butanols); 0 (Hydroxybenzoic Acids); 0 (Triglycerides); EC 2.6.1.1 (Aspartate Aminotransferases); EC 2.6.1.2 (Alanine Transaminase)

L215 ANSWER 19 OF 30 MEDLINE on STN DUPLICATE 13

ACCESSION NUMBER: 89227627 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2712711

TITLE: Hypolipemic activity of K12.148 in rats, marmosets and pigs.

AUTHOR: Schliack M; **Loser R**; **Seibel K**; Blay K H

CORPORATE SOURCE: Klinge Pharma GmbH, Department of Biochemical Research, Munich, F.R.G.

SOURCE: Artery, (1989) 16 (2) 90-104.
Journal code: 7508494. ISSN: 0098-6127.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198906

ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890608

ABSTRACT:
The hypolipemic effect of K12.148, a new hypolipemic compound, was examined in normolipemic rats, marmosets and pigs. It could be demonstrated that this compound reduced serum lipids, and in particular serum cholesterol, very effectively in all tested animal species. The analysis of the lipids of the pig give evidence that the hypocholesterolemic effect is due to a reduction of LDL only. In vitro experiments with rat liver homogenates suggest that the hypocholesterolemic effect is brought about by the inhibition of hepatic

cholesterol synthesis.
CONTROLLED TERM: Check Tags: Female; Male
Animals
Butanols: AD, administration & dosage
*Butanols: PD, pharmacology
Callithrix
Cholesterol: BI, biosynthesis
*Cholesterol: BL, blood
Hydroxybenzoic Acids: AD, administration & dosage
*Hydroxybenzoic Acids: PD, pharmacology
*Lipoproteins, LDL Cholesterol: BL, blood
Liver: DE, drug effects
Liver: ME, metabolism
Rats
Rats, Inbred Strains
Swine
*Triglycerides: BL, blood
CAS REGISTRY NO.: 57-88-5 (Cholesterol); 96609-16-4 (lifibrol)
CHEMICAL NAME: 0 (Butanols); 0 (Hydroxybenzoic Acids); 0 (Lipoproteins, LDL Cholesterol); 0 (Triglycerides)

L215 ANSWER 20 OF 30 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 89117070 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3218958
TITLE: Pharmacological activities of droloxifene isomers.
AUTHOR: **Loser R**; **Seibel K**; Huber H J
CORPORATE SOURCE: Klinge Pharma GmbH, Munich, F.R.G.
SOURCE: Anticancer research, (1988 Nov-Dec) 8 (6) 1271-4.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198903
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19890306

ABSTRACT:
Droloxifene (DROL) is a new antiestrogen which is used for the treatment of endocrine-responsive breast cancer in humans. As Droloxifene exists in a Z- and E-isomer, we investigated the main pharmacological properties of both isomers. For both compounds the following tests were conducted: affinity for the estrogen receptor (ER); effect on the growth of rat uteri; influence on the growth of the ER + human breast cancer cell line ZR-75; and isomer interconversion in vitro. DROL-(Z) had binding affinity to the cytosolic ER approximately ten times lower than that of DROL-(E). Furthermore, the estrogenic effect of DROL-(Z) in the rat uterus is weak and there is no antiestrogenic activity. The lack of antiestrogenic activity of DROL-(Z) in contrast to DROL-(E) could also be shown in the human breast cancer cells ZR-75. Thus DROL-(Z) is, as far as investigated, without antiestrogenic and estrogenic activities. Of note is the stability of both DROL-isomers. There is no interconversion or metabolism of the parent compounds DROL-(E) and DROL-(Z) in vitro.
CONTROLLED TERM: Check Tags: Female
Animals
Binding, Competitive
Cell Division: DE, drug effects
Cell Line
*Estrogen Antagonists: PD, pharmacology
Humans

Isomerism
Kinetics
Organ Size: DE, drug effects
RNA, Neoplasm: BI, biosynthesis
RNA, Neoplasm: DE, drug effects
Receptors, Estradiol: DE, drug effects
Receptors, Estradiol: ME, metabolism
*Tamoxifen: AA, analogs & derivatives
Tamoxifen: PD, pharmacology
Uterus: AH, anatomy & histology
Uterus: DE, drug effects

CAS REGISTRY NO.: 10540-29-1 (Tamoxifen); 82413-20-5 (3-hydroxytamoxifen)
CHEMICAL NAME: 0 (Estrogen Antagonists); 0 (RNA, Neoplasm); 0 (Receptors, Estradiol)

L215 ANSWER 21 OF 30 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 87270960 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3606713
TITLE: Circadian variation of the hypocholesterolemic effect of K13.004 in rats.
AUTHOR: Schliack M; **Loser R**; **Seibel K**
SOURCE: Atherosclerosis, (1987 Apr) 64 (2-3) 163-6.
Journal code: 0242543. ISSN: 0021-9150.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198707
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19980206
Entered Medline: 19870724

ABSTRACT:
The hypocholesterolemic effect in rats of the new lipid-lowering agent K13.004 was dependent on the time of day of its application. This dependence was shifted together with the time of peak activity of hepatic cholesterol synthesis (CS) when the feeding time of the animals was changed. This compound considerably reduced serum cholesterol only if given before the peak of hepatic CS, whereas application afterwards was ineffective. Our finding suggests that this hypolipidemic compound lowers serum cholesterol by inhibition of hepatic CS. Drugs acting in such a way should be administered prior to the maximum of hepatic sterol synthesis.

CONTROLLED TERM: Check Tags: Male
1-Propanol: PD, pharmacology
Animals
*Anticholesteremic Agents: PD, pharmacology
*Cholesterol: BL, blood
*Circadian Rhythm
*Propanols
Rats
Rats, Inbred Strains

CAS REGISTRY NO.: 57-88-5 (Cholesterol); 71-23-8 (1-Propanol); 96609-38-0 (K 13-004)
CHEMICAL NAME: 0 (Anticholesteremic Agents); 0 (Propanols)

L215 ANSWER 22 OF 30 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 86004906 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4043181
TITLE: In vivo and in vitro antiestrogenic action of 3-hydroxytamoxifen, tamoxifen and 4-hydroxytamoxifen.
AUTHOR: **Loser R**; **Seibel K**; Roos W; Eppenberger

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SOURCE: European journal of cancer & clinical oncology, (1985 Aug) 21 (8) 985-90.
Journal code: 8112045. ISSN: 0277-5379.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198510
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19851028

ABSTRACT:
This study demonstrates in vivo and in vitro properties of the non-steroidal antiestrogens tamoxifen (TAM), 4-OH-tamoxifen (4-OH-TAM) and 3-OH-tamoxifen (K 060 E). In immature rabbit uteri 4-OH-TAM and K 060 E bound to the respective estrogen receptors with a ten-fold higher affinity than TAM. Furthermore, K 060 E exhibited less agonistic (estrogenic) but higher antagonistic (antiestrogenic) activity in the immature rat uterus than TAM and 4-OH-TAM (change of uterine weight). The ratio of agonistic vs antagonistic effect of K 060 E was distinctly lower than in TAM and 4-OH-TAM. In addition, K 060 E reduced by approximately 45% the growth of the transplantable Fisher rat mammary tumor (R 3230 AC) as compared with TAM (33%). We assume that, due to the higher antitumor activity, K 060 E (3-OH-TAM) is a better antiestrogen than TAM.

CONTROLLED TERM: Check Tags: Female
Adenocarcinoma: DT, drug therapy
Animals
Binding, Competitive
Dose-Response Relationship, Drug
Estradiol: ME, metabolism
*Estrogen Antagonists: PD, pharmacology
Mammary Neoplasms, Experimental: DT, drug therapy
Organ Size: DE, drug effects
Rabbits
Rats
Rats, Inbred Strains
Receptors, Estrogen: ME, metabolism
Research Support, Non-U.S. Gov't
*Tamoxifen: AA, analogs & derivatives
*Tamoxifen: PD, pharmacology
Tamoxifen: TU, therapeutic use
*Uterus: DE, drug effects
Uterus: ME, metabolism
CAS REGISTRY NO.: 10540-29-1 (Tamoxifen); 50-28-2 (Estradiol); 68392-35-8 (4-hydroxytamoxifen); 82413-20-5 (3-hydroxytamoxifen)
CHEMICAL NAME: 0 (Estrogen Antagonists); 0 (Receptors, Estrogen)

L215 ANSWER 23 OF 30 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 86058139 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4066073
TITLE: No loss of estrogenic or anti-estrogenic activity after demethylation of droloxifene (3-OH-tamoxifen).
AUTHOR: **Loser R**; **Seibel K**; Eppenberger U
SOURCE: International journal of cancer. Journal international du cancer, (1985 Dec 15) 36 (6) 701-3.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 198601
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860114

ABSTRACT:
The binding affinity of 3-OH-Tamoxifen (Droloxifene or DROL) and N-demethyl-droloxifene (ND-DROL) to the cystosolic estrogen receptor of rabbit uteri was 10 times higher than that of Tamoxifen. Both compounds exhibited similar stimulation (estrogenic effect) and inhibition (anti-estrogenic effect) of uterine growth of immature female rats. 3H-Uridine incorporation into the RNA of MCF-7 and ZR-75 cells as a measure of anti-estrogenic activity was equally inhibited by concentrations of 0.05-1.0 mumol/l of both compounds. Thus, the pharmacological properties of DROL were not changed by N-demethylation.

CONTROLLED TERM: Check Tags: Female
Animals
Binding, Competitive
Breast Neoplasms
Cell Division: DE, drug effects
Cell Line
*Estrogen Antagonists: ME, metabolism
Estrogen Antagonists: PD, pharmacology
Humans
Methylation
Rats
*Receptors, Estrogen: ME, metabolism
Research Support, Non-U.S. Gov't
*Tamoxifen: AA, analogs & derivatives
Tamoxifen: ME, metabolism
Tamoxifen: PD, pharmacology
Uterus: DE, drug effects
Uterus: ME, metabolism

CAS REGISTRY NO.: 10540-29-1 (Tamoxifen); 82413-20-5 (3-hydroxytamoxifen); 83647-33-0 (N-demethyldroloxifene)
CHEMICAL NAME: 0 (Estrogen Antagonists); 0 (Receptors, Estrogen)

L215 ANSWER 24 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2003516791 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14594650
TITLE: Poly ADP-ribose polymerase (PARP) inhibitors transiently protect leukemia cells from alkylating agent induced cell death by three different effects.
AUTHOR: Pogrebniak A; **Schemainda I**; Pelka-Fleischer R; Nussler V; **Hasmann M**
CORPORATE SOURCE: Department of Haematology and Oncology, Klinikum Grosshadern, Munich, Germany.
SOURCE: European journal of medical research, (2003 Oct 22) 8 (10) 438-50.
Journal code: 9517857. ISSN: 0949-2321.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20031104
Last Updated on STN: 20040625
Entered Medline: 20040623

ABSTRACT:
Polyadenosylation of nuclear enzymes is well known to regulate the cellular

repair capacity after DNA damage. PARP mediates the transfer of poly-ADP-ribose moieties on itself and other nuclear proteins by the breakdown of NAD+. The present study investigated how modulation of PARP activity interferes with cell death induced by two different alkylating agents used in cancer chemotherapy. 1-methyl-3-nitro-1-nitrosoguanidinium (MNNG) decreased cellular reduction capacity (WST-1 assay) in HL60 and CCRF-CEM cells, accompanied by increased activity of PARP and depletion of intracellular NAD+ and ATP. Pretreatment with the PARP inhibitors 3-AB or 4-AN resulted in transient cell protection, which was associated with a switch from necrosis to apoptosis in CCRF-CEM cells and enhanced apoptosis in HL60 cells. Both PARP inhibitors delayed the drop in WST-1 reduction and retained NAD+ and ATP levels required for apoptosis. Furthermore, 3-AB or 4-AN prevented progressive DNA degradation in MNNG-treated CCRF-CEM cells. In contrast to MNNG, we did not observe early activation of PARP, decrease in WST-1 reduction, or wasteful consumption of NAD+ and ATP after treatment with melphalan. However, preincubation with 3-AB or 4-AN resulted in decreased HL60 cell membrane blebbing and reduced formation of apoptotic bodies. In conclusion, the cell death preventing effects of PARP inhibitors are mediated by their ability to maintain cellular energy metabolism, to inhibit the activation of endonucleolytic DNA degradation and to prevent cell blebbing. Surprisingly, these protective effects of PARP inhibitors on different cell functions seem to be independent of each other and are rather determined by the respective cytotoxic mechanisms implicated by different drugs. Our results support the hypothesis, that PARP activation and/or cleavage plays a regulatory role in the induction of apoptosis.

CONTROLLED TERM: *1-Naphthylamine: AA, analogs & derivatives
1-Naphthylamine: PD, pharmacology
Adenosine Triphosphate: ME, metabolism
*Alkylating Agents: AI, antagonists & inhibitors
*Alkylating Agents: PD, pharmacology
Apoptosis: DE, drug effects
Benzamides: PD, pharmacology
Cell Death: DE, drug effects
Cell Line, Tumor
Cell Size: DE, drug effects
*Enzyme Inhibitors: PD, pharmacology
HL-60 Cells
Humans
Leukemia: DT, drug therapy
Leukemia: ME, metabolism
*Leukemia: PA, pathology
Melphalan: PD, pharmacology
Methylnitronitrosoguanidine: PD, pharmacology
NAD: ME, metabolism
*Poly(ADP-ribose) Polymerases: AI, antagonists & inhibitors
Poly(ADP-ribose) Polymerases: ME, metabolism
Quinolones: PD, pharmacology

CAS REGISTRY NO.: 134-32-7 (1-Naphthylamine); 148-82-3 (Melphalan); 1742-95-6 (4-amino-1,8-naphthalimide); 3544-24-9 (3-aminobenzamide); 53-84-9 (NAD); 56-65-5 (Adenosine Triphosphate); 70-25-7 (Methylnitronitrosoguanidine)

CHEMICAL NAME: 0 (Alkylating Agents); 0 (Benzamides); 0 (Enzyme Inhibitors); 0 (Quinolones); EC 2.4.2.30 (Poly(ADP-ribose) Polymerases)

L215 ANSWER 25 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2002405276 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12121133
TITLE: Polyethylene glycol conjugates of methotrexate varying in their molecular weight from MW 750 to MW 40000: synthesis,

characterization, and structure-activity relationships in vitro and in vivo.

AUTHOR: Riebeseel Katja; **Biedermann Elfi**; **Loser Roland**; Breiter Norbert; Hanselmann Ralf; Mulhaupt Rolf; Unger Clemens; Kratz Felix

CORPORATE SOURCE: Tumor Biology Center, Department of Medical Oncology, Clinical Research, Breisacher Strasse 117, 79106 Freiburg, Germany.

SOURCE: Bioconjugate chemistry, (2002 Jul-Aug) 13 (4) 773-85. Journal code: 9010319. ISSN: 1043-1802.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200308

ENTRY DATE: Entered STN: 20020806
Last Updated on STN: 20021212
Entered Medline: 20030805

ABSTRACT:
Poly(ethylene glycol)s (PEGs) are potential drug carriers for improving the therapeutic index of anticancer agents. In this work, the anticancer drug methotrexate (MTX) was activated with N,N'-dicyclohexylcarbodiimide (DCC) and coupled to amino group bearing PEGs of MW 750, 2000, 5000, 10 000, 20,000, and 40,000. First, the activation process of MTX with DCC in the presence and absence of N-hydroxysuccinimide was analyzed through HPLC. Preincubation of methotrexate with DCC alone at 0 degrees C proved to be favorable with respect to the amount of activated species and the formation of byproducts. MTX-PEG conjugates were synthesized according to this procedure, isolated through size-exclusion chromatography, and characterized through analytical HPLC, MALDI-TOF spectrometry, and gel permeation chromatography. In a cell-free assay, all of the drug polymer conjugates inhibited the target enzyme of MTX, dihydrofolate reductase (DHFR), to a similar extent, but were not as active as free MTX. Additionally, incubation of the MTX-PEG40000 conjugate for 6 days at 37 degrees C in phosphate buffered saline (pH 7.4), in cell-conditioned medium, or in human serum revealed no significant release of methotrexate. These results, taken together, indicate that release of MTX from polymer conjugates is not necessary for an effective interaction with the active site of dihydrofolate reductase. Evaluation of the in vitro cytotoxicity of the MTX-PEG conjugates in two adherent and three suspension human tumor cell lines revealed that the IC(50) values of the tested compounds increased with the size of the drug-polymer conjugates. The most effective compound tested in these assays was the free drug MTX itself (IC(50) value ranging from approximately 0.01 to 0.05 microM), while the IC(50) values of the polymer conjugates were higher (IC(50) value for MTX-PEG750, 2000 and 5000: approximately 0.6-3 microM; for MTX-PEG10000 and 20000: approximately 2-7 microM; and for MTX-PEG40000: > 6 microM). Subsequently, MTX-PEG5000, MTX-PEG20000, and MTX-PEG40000 were evaluated in a human mesothelioma MSTO-211H xenograft model, and their antitumor effects were compared with free methotrexate and the albumin conjugate MTX-HSA, a conjugate that is currently in phase II clinical trials. In contrast to the in vitro results, the high molecular weight MTX-PEG conjugates exhibited the highest in vivo antitumor activity: At a dose of 40 and 80 mg/kg MTX-PEG5000 was less active than MTX at its optimal dose of 100 mg/kg; MTX-PEG20000 at a dose of 40 mg/kg showed antitumor efficacy comparable to MTX, but MTX-PEG40000 at a dose of 20 mg/kg was superior to MTX and demonstrated antitumor activity of the same order as MTX-HSA (20 mg/kg).

CONTROLLED TERM: Check Tags: Female
Animals
*Antimetabolites, Antineoplastic: AD, administration & dosage
Antimetabolites, Antineoplastic: CH, chemistry

Cell Division: DE, drug effects
Cross-Linking Reagents: CH, chemistry
Dose-Response Relationship, Drug
Drug Carriers: CH, chemistry
Drug Carriers: TU, therapeutic use
Drug Evaluation, Preclinical
Humans
Inhibitory Concentration 50
*Methotrexate: AD, administration & dosage
Methotrexate: CH, chemistry
Methotrexate: PD, pharmacology
Mice
Mice, Nude
Molecular Weight
Neoplasms, Experimental: DT, drug therapy
*Polyethylene Glycols: CH, chemistry
Polyethylene Glycols: TU, therapeutic use
Structure-Activity Relationship
Tetrahydrofolate Dehydrogenase: DE, drug effects
Transplantation, Heterologous
Tumor Cells, Cultured

CAS REGISTRY NO.: 59-05-2 (Methotrexate)
CHEMICAL NAME: 0 (Antimetabolites, Antineoplastic); 0 (Cross-Linking Reagents); 0 (Drug Carriers); 0 (Polyethylene Glycols); EC 1.5.1.3 (Tetrahydrofolate Dehydrogenase)

L215 ANSWER 26 OF 30 EMBASE
ACCESSION NUMBER: 94110489 EMBASE
DOCUMENT NUMBER: 1994110489
TITLE: [Inhibition of growth factor induced proliferation of MCF-7 breast cancer cells by means of antiestrogens and effects on protooncogene activation].
HEMMUNG DER WACHSTUMSFAKTOR-INDUZIERTEN PROLIFERATION VON MCF-7-MAMMAKARZINOMZELLEN DURCH ANTIOSTROGENE UND EFFEKTE AUF PROTOONKOLOGEN-AKTIVIERUNGEN.
AUTHOR: Kung W.; **Wosikowski K.**; **Hasmann M.**; **Loser R.**; Eppenberger U.
CORPORATE SOURCE: Kantonsspital, Departement Forschung, Hebelstrasse 20,CH-4031 Basel, Switzerland
SOURCE: Onkologie, (1994) Vol. 17, No. SUPPL. 1, pp. 27-31.
ISSN: 0378-584X CODEN: ONKOD2
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: German; English
ENTRY DATE: Entered STN: 940504
Last Updated on STN: 940504

ABSTRACT: The antitumor effect of antiestrogens is thought to be mainly associated with the potency of the antiestrogens to compete for estradiol at the estrogen receptors of the cancer cells. Recently, it was found that antiestrogens are also able to inhibit the proliferation of growth factor-stimulated estrogen receptor-positive breast cancer cells MCF-7. Results of similar work in other laboratories were not consistent. Therefore, we have also performed analogous experiments but, in contrast to the other studies, under entirely defined serum- and estrogen-free culture conditions.

Epidermal growth factor (EGF) and insulin-like growth factor type I (IGF-I) were used as mitogens. For MCF-7 cells, EGF is a weak and IGF-I is a strong mitogen. A comparison between tamoxifen and the new antiestrogen droloxifene showed that both antiestrogens inhibit EGF- as well as IGF-I-induced proliferation of MCF-7 cells. Under all conditions, droloxifene was a considerably more potent growth inhibitor than tamoxifen. Because the mechanism of this growth factor-related antiproliferative activity of antiestrogens is not yet clear, we have studied whether they influence the regulation of the protooncogenes c-fos and c-myc. The results obtained do not favor this hypothesis.

CONTROLLED TERM: Medical Descriptors:
*breast cancer
*proto oncogene
article
cell strain mcf 7
controlled study
growth inhibition
human
human cell
Drug Descriptors:
*droloxifene: CB, drug combination
*droloxifene: CM, drug comparison
*droloxifene: IT, drug interaction
*droloxifene: PD, pharmacology
*epidermal growth factor: PD, pharmacology
*epidermal growth factor: IT, drug interaction
*epidermal growth factor: CB, drug combination
*epidermal growth factor: CM, drug comparison
*somatomedin c: CM, drug comparison
*somatomedin c: IT, drug interaction
*somatomedin c: PD, pharmacology
*somatomedin c: CB, drug combination
*tamoxifen: PD, pharmacology
*tamoxifen: IT, drug interaction
*tamoxifen: CM, drug comparison
*tamoxifen: CB, drug combination

CAS REGISTRY NO.: (droloxifene) 82413-20-5; (epidermal growth factor) 62229-50-9; (somatomedin c) 67763-96-6; (tamoxifen) 10540-29-1

COMPANY NAME: Collaborative research (United States); Boehringer (Germany); Klinge pharma (Germany); Ici (United Kingdom)

L215 ANSWER 27 OF 30 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 94110488 EMBASE

DOCUMENT NUMBER: 1994110488

TITLE: [Growth inhibition of human tumor cells by means of intermittent treatment with droloxifene]. WACHSTUMSHEMMUNG VON MENSCHLICHEN TUMORZELLEN DURCH INTERMITTIERENDE BEHANDLUNG MIT DROLOXIFEN.

AUTHOR: **Hasmann M.**; **Loser R.**; Kohr A.; **Seibel K.**

CORPORATE SOURCE: Klinge Pharma GmbH, Abteilung Pharmakologie, Postfach 801063,D-81610 Munchen, Germany

SOURCE: Onkologie, (1994) Vol. 17, No. SUPPL. 1, pp. 22-26. ISSN: 0378-584X CODEN: ONKOD2

COUNTRY: Germany

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer

037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: German; English
ENTRY DATE: Entered STN: 940511
Last Updated on STN: 940511

ABSTRACT: The new antiestrogen droloxifene (DROL) is pharmacokinetically distinguished from tamoxifen (TAM) by its rapid uptake, low accumulation, and a short elimination half-life. These characteristics predispose DROL for an intermittent therapy regimen, which may prevent acquisition of drug resistance and further decrease potential side effects of adjuvant long-term therapy. We evaluated the effects of short-term and intermittent application of DROL and TAM on human tumor cell lines measuring DNA content in culture dishes by the Burton reagent method. In both estrogen receptor(ER)-positive breast cancer cell lines, ZR-75-1 and MCF-7 M1, DROL acted much faster than TAM, which is consistent with a more rapid uptake kinetics. DROL needed only 15-30 min incubation time in order to display its full antiproliferative effect, while at least 2 h were required for TAM, which in addition was clearly less effective. A single 2-hour incubation period of MCF-7 M1 cells with DROL entirely inhibited cell growth for up to 11 days. In vitro simulation of an intermittent therapy regimen by 2-hour treatment intervals every 3rd day resulted in complete growth inhibition of MCF-7 M1 cells over more than 3 weeks. Comparison with DROL revealed that both TAM and another antiestrogen, toremifene, were at least 10 times weaker antiproliferative agents for ER-positive cells, and the difference was further enlarged when short drug incubation times were applied. In conclusion, because of its rapid uptake and its sustaining cell growth inhibition after short-time application of therapeutically relevant concentrations, DROL may be the first antiestrogen suitable for an intermittent hormonal therapy regimen of breast cancer patients.

CONTROLLED TERM: Medical Descriptors:
*breast cancer
cell strain mcf 7
conference paper
controlled study
growth inhibition
human
human cell
Drug Descriptors:
*droloxifene: PD, pharmacology
*droloxifene: DO, drug dose
*droloxifene: CM, drug comparison
*tamoxifen: PD, pharmacology
*tamoxifen: DO, drug dose
*tamoxifen: CM, drug comparison
CAS REGISTRY NO.: (droloxifene) 82413-20-5; (tamoxifen) 10540-29-1

L215 ANSWER 28 OF 30 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 94110487 EMBASE
DOCUMENT NUMBER: 1994110487
TITLE: [Droloxifene inhibits growth and protein synthesis of breast cancer cells more effectively than tamoxifen and toremifene].
DROLOXIFEN HEMMT DAS WACHSTUM UND DIE PROTEINSYNTHESE VON BRUSTKREBSZELLEN EFFEKTIVER ALS TAMOXIFEN UND TOREMIFEN.
AUTHOR: **Biedermann E.; Loser R.; Hasmann M.**
CORPORATE SOURCE: Klinge Pharma GmbH, Postfach 801063,D-81610 Munchen, Germany

SOURCE: Onkologie, (1994) Vol. 17, No. SUPPL. 1, pp. 17-21.
ISSN: 0378-584X CODEN: ONKOD2
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: German; English
ENTRY DATE: Entered STN: 940504
Last Updated on STN: 940504

ABSTRACT: The new triphenylethylene antiestrogen droloxifene (DROL) is distinguished from tamoxifen (TAM) and toremifene (TOR) by a more than 10-fold higher binding affinity to the human estrogen receptor (ER). The present study was carried out to test whether this high affinity binding translated into increased effects on cell growth and protein synthesis. We compared the antiproliferative potency of the antiestrogens DROL, TAM and TOR on the ER-positive cell line MCF-7 M1 under serum-free conditions. The effects on cellular protein biosynthesis were determined by 14C-leucine incorporation, and by flow cytometry after staining cellular proteins with sulforhodamine 101. The IC50 value for MCF-7 M1 cell growth inhibition was found to be less than 0.03 μM for DROL. In contrast, the dose-response curves of both TAM and TOR were shifted to at least 10-fold higher concentrations. DROL concentrations between 0.03 and 1 μM, which produce no ER-independent effects, reduced the incorporation of 14C leucine dose-dependently with a similar efficacy as cycloheximide, a well-known inhibitor of eukaryotic protein biosynthesis. Equimolar concentrations of TAM or TOR had no effect. Similar results were obtained by flow cytometric quantitation of cellular protein content. In conclusion, the high affinity binding of DROL to the ER is correlated by superior antiproliferative activity as compared to TAM and TOR. Surprisingly, DROL compares well with cycloheximide as an inhibitor of protein synthesis in ER-positive breast cancer cells; in contrast, TAM and TOR are without effect when tested in therapeutically relevant concentrations.

CONTROLLED TERM: Medical Descriptors:
*breast cancer
conference paper
controlled study
growth inhibition
human
human cell
protein synthesis inhibition
Drug Descriptors:
*droloxifene: PD, pharmacology
*droloxifene: DO, drug dose
*droloxifene: CM, drug comparison
*tamoxifen: PD, pharmacology
*tamoxifen: DO, drug dose
*tamoxifen: CM, drug comparison
*toremifene: PD, pharmacology
*toremifene: DO, drug dose
*toremifene: CM, drug comparison
CAS REGISTRY NO.: (droloxifene) 82413-20-5; (tamoxifen) 10540-29-1; (toremifene) 89778-26-7

L215 ANSWER 29 OF 30 EMBASE
ACCESSION NUMBER: 88129643 EMBASE
DOCUMENT NUMBER: 1988129643
TITLE: Inhibition of growth of human cancer by intermittent

exposure to the antiestrogen droloxifene.
AUTHOR: Ahlemann L.M.; Staab H.-J.; **Loser R.**; **Seibel K.**; Huber H.-J.
CORPORATE SOURCE: Strahlentherapeutische Abteilung, Kreiskrankenhaus Ludenscheid, D-5880 Ludenscheid, Germany
SOURCE: Tumor Diagnostik und Therapie, (1988) Vol. 9, No. 2, pp. 41-46.
ISSN: 0722-219X CODEN: TDTHDB
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: German
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211
CONTROLLED TERM: Medical Descriptors:
*breast cancer: DT, drug therapy
cell culture
clinical article
human cell
human
female
oral drug administration
Drug Descriptors:
*antiestrogen
*droloxifene: PD, pharmacology
*droloxifene: CT, clinical trial
CAS REGISTRY NO.: (droloxifene) 82413-20-5
COMPANY NAME: Klinge pharma (Germany)

L215 ANSWER 30 OF 30 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 84094910 EMBASE
DOCUMENT NUMBER: 1984094910
TITLE: K-21060 E.
AUTHOR: **Loser R.**; Janiak -St. P.; **Seibel K.**
CORPORATE SOURCE: Switzerland
SOURCE: Drugs of the Future, (1984) Vol. 9, No. 3, pp. 186-188.
CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210
CONTROLLED TERM: Medical Descriptors:
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*cancer chemotherapy
*cell strain zr 75
*dose response
*drug comparison
*drug cytotoxicity
*drug efficacy
*drug identification
*drug receptor binding
*drug screening
*drug synthesis
*drug toxicity

*cell strain mcf 7
*uterus weight
drug analysis
drug response
pharmacokinetics
therapy
intoxication
female genital system
intravenous drug administration
oral drug administration
short survey
human cell
animal experiment
animal cell
in vitro study
animal model
human
mouse
rat
breast
Drug Descriptors:
*droloxifene
estradiol
tamoxifen
new drug
k 21060 e
unclassified drug

CAS REGISTRY NO.: (droloxifene) 82413-20-5; (estradiol) 50-28-2; (tamoxifen) 10540-29-1
CHEMICAL NAME: K 21060 e
COMPANY NAME: Klinge pharma (Germany)

=>

=> □

TEXT/STRUCTURE Search

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=> file caplus
FILE 'CAPLUS' ENTERED AT 17:11:17 ON 26 OCT 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 26 Oct 2005  VOL 143 ISS 18
FILE LAST UPDATED: 25 Oct 2005  (20051025/ED)

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http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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                  PKT OR THU)/RL
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=> d que nos L44

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L9                STR
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L35            17 SEA FILE=CAPLUS ABB=ON  PLU=ON  L22 AND L19 AND ((L17 OR L18))

L42          7755 SEA FILE=CAPLUS ABB=ON  PLU=ON  CHEMOTHERAPY/CT
L44             3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L35 AND L42


=> s (L32 or L39 or l43 or l44) not L213
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L216 12 (L32 OR L39 OR L43 OR L44) NOT L213 previously printed with author search

=> file medline

FILE 'MEDLINE' ENTERED AT 17:11:21 ON 26 OCT 2005

FILE LAST UPDATED: 25 OCT 2005 (20051025/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos L107

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L84       85537 SEA FILE=MEDLINE ABB=ON  PLU=ON  L80 (L) AE/CT
L86      626924 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?TOXIC?
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L92        1866 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACIN/CT
L94        4762 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACINAMIDE/CT
L105       3847 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L91 OR L92 OR L94) (L) (TU
                OR AD)/CT
L106         30 SEA FILE=MEDLINE ABB=ON  PLU=ON  L105 AND L84
L107          5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 AND L86
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=> d que nos L110

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L86      626924 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?TOXIC?
L91        5513 SEA FILE=MEDLINE ABB=ON  PLU=ON  NICOTINIC ACIDS/CT
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L94        4762 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACINAMIDE/CT
L105       3847 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L91 OR L92 OR L94) (L) (TU
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L108         25 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 NOT L107
L109    1450721 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEOPLAS?
L110          2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L108 AND L109
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=> d que nos L116

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               RESSIVE AGENTS"+NT/CT
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L86        626924 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?TOXIC?
L91          5513 SEA FILE=MEDLINE ABB=ON  PLU=ON  NICOTINIC ACIDS/CT
L92          1866 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACIN/CT
L94          4762 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACINAMIDE/CT
L105         3847 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L91 OR L92 OR L94) (L) (TU
               OR AD)/CT
L106           30 SEA FILE=MEDLINE ABB=ON  PLU=ON  L105 AND L84
L107            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 AND L86
L108           25 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 NOT L107
L109      1450721 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEOPLAS?
L110            2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L108 AND L109
L114          564 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L91 OR L92 OR L94) (L) AE/CT

L115           14 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 NOT L114
L116            9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L115 NOT (L107 OR L110)


=> d que nos L125

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L6                STR
L8            387 SEA FILE=REGISTRY FAM FUL L6
L9                STR
L11         11383 SEA FILE=REGISTRY SSS FUL L9
L65          8330 SEA FILE=MEDLINE ABB=ON  PLU=ON  L4
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L91          5513 SEA FILE=MEDLINE ABB=ON  PLU=ON  NICOTINIC ACIDS/CT
L92          1866 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACIN/CT
L94          4762 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACINAMIDE/CT
L112          100 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 AND MEDLINE/LC
L113        11465 SEA FILE=MEDLINE ABB=ON  PLU=ON  L112
L118         7037 SEA FILE=MEDLINE ABB=ON  PLU=ON  ((L65 OR L66) ) NOT (L91 OR
               L92 OR L94)
L119        18410 SEA FILE=MEDLINE ABB=ON  PLU=ON  L118 OR L113
L122         5654 SEA FILE=MEDLINE ABB=ON  PLU=ON  CYTOPROTECT?
L124            2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L119 AND L122
L125            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L124 AND TUMOR


=> d que nos L132

L2                STR
L4            745 SEA FILE=REGISTRY FAM FUL L2
L6                STR
L8            387 SEA FILE=REGISTRY FAM FUL L6
L9                STR
L11         11383 SEA FILE=REGISTRY SSS FUL L9
L65          8330 SEA FILE=MEDLINE ABB=ON  PLU=ON  L4
L66          5443 SEA FILE=MEDLINE ABB=ON  PLU=ON  L8
L80        657410 SEA FILE=MEDLINE ABB=ON  PLU=ON  "ANTINEOPLASTIC AND IMMUNOSUPP
               RESSIVE AGENTS"+NT/CT
L84          85537 SEA FILE=MEDLINE ABB=ON  PLU=ON  L80 (L) AE/CT
L86         626924 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?TOXIC?
L91           5513 SEA FILE=MEDLINE ABB=ON  PLU=ON  NICOTINIC ACIDS/CT
L92           1866 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACIN/CT
L94           4762 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACINAMIDE/CT
L105          3847 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L91 OR L92 OR L94) (L) (TU
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                OR AD)/CT
L106          30 SEA FILE=MEDLINE ABB=ON  PLU=ON  L105 AND L84
L107           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 AND L86
L108          25 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 NOT L107
L109     1450721 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEOPLAS?
L110           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L108 AND L109
L112         100 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 AND MEDLINE/LC
L113       11465 SEA FILE=MEDLINE ABB=ON  PLU=ON  L112
L114         564 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L91 OR L92 OR L94) (L) AE/CT

L115          14 SEA FILE=MEDLINE ABB=ON  PLU=ON  L106 NOT L114
L116           9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L115 NOT (L107 OR L110)
L118        7037 SEA FILE=MEDLINE ABB=ON  PLU=ON  ((L65 OR L66) ) NOT (L91 OR
                L92 OR L94)
L119       18410 SEA FILE=MEDLINE ABB=ON  PLU=ON  L118 OR L113
L120          35 SEA FILE=MEDLINE ABB=ON  PLU=ON  L84 AND L119
L122        5654 SEA FILE=MEDLINE ABB=ON  PLU=ON  CYTOPROTECT?
L124           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L119 AND L122
L125           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L124 AND TUMOR
L128        2578 SEA FILE=MEDLINE ABB=ON  PLU=ON  PYRIDOXINE/CT (L) (TU OR
                AD)/CT
L129          28 SEA FILE=MEDLINE ABB=ON  PLU=ON  L120 AND L128
L130          35 SEA FILE=MEDLINE ABB=ON  PLU=ON  L120 NOT (L107 OR L110 OR
                L116 OR L125)
L131           7 SEA FILE=MEDLINE ABB=ON  PLU=ON  L130 NOT L129
L132           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L131 AND ANTINEOPLASTIC


=> d que nos L135

L2                STR
L4            745 SEA FILE=REGISTRY FAM FUL L2
L6                STR
L8            387 SEA FILE=REGISTRY FAM FUL L6
L9                STR
L11         11383 SEA FILE=REGISTRY SSS FUL L9
L65          8330 SEA FILE=MEDLINE ABB=ON  PLU=ON  L4
L66          5443 SEA FILE=MEDLINE ABB=ON  PLU=ON  L8
L80        657410 SEA FILE=MEDLINE ABB=ON  PLU=ON  "ANTINEOPLASTIC AND IMMUNOSUPP
                RESSIVE AGENTS"+NT/CT
L84          85537 SEA FILE=MEDLINE ABB=ON  PLU=ON  L80 (L) AE/CT
L91           5513 SEA FILE=MEDLINE ABB=ON  PLU=ON  NICOTINIC ACIDS/CT
L92           1866 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACIN/CT
L94           4762 SEA FILE=MEDLINE ABB=ON  PLU=ON  NIACINAMIDE/CT
L112           100 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 AND MEDLINE/LC
L113         11465 SEA FILE=MEDLINE ABB=ON  PLU=ON  L112
L118          7037 SEA FILE=MEDLINE ABB=ON  PLU=ON  ((L65 OR L66) ) NOT (L91 OR
                L92 OR L94)
L119         18410 SEA FILE=MEDLINE ABB=ON  PLU=ON  L118 OR L113
L120            35 SEA FILE=MEDLINE ABB=ON  PLU=ON  L84 AND L119
L128          2578 SEA FILE=MEDLINE ABB=ON  PLU=ON  PYRIDOXINE/CT (L) (TU OR
                AD)/CT
L133        192654 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTINEOPLASTIC
L135            11 SEA FILE=MEDLINE ABB=ON  PLU=ON  L133 AND L120 AND L128


=> s (L107 or l110 or l116 or l125 or l132 or L135) not L214

L217            29 (L107 OR L110 OR L116 OR L125 OR L132 OR L135) NOT L214
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previously printed with author search

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=> file embase

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 FILE COVERS 1974 TO 20 Oct 2005 (20051020/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos L188

L166     259655 SEA FILE=EMBASE ABB=ON  PLU=ON  IMMUNOSUPPRESSIVE AGENT+NT/CT
L167     600211 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENT+NT/CT
L169       7811 SEA FILE=EMBASE ABB=ON  PLU=ON  NICOTINIC ACID/CT
L170       4321 SEA FILE=EMBASE ABB=ON  PLU=ON  NICOTINAMIDE/CT
L174      86419 SEA FILE=EMBASE ABB=ON  PLU=ON  ((L166 OR L167)) (L) AE/CT
L176     149971 SEA FILE=EMBASE ABB=ON  PLU=ON  CHEMOTHERAPY+NT/CT
L183       3557 SEA FILE=EMBASE ABB=ON  PLU=ON  ((L169 OR L170)) (L) (DT OR AD
                  OR DO)/CT
L184        180 SEA FILE=EMBASE ABB=ON  PLU=ON  L183 AND L174
L185         11 SEA FILE=EMBASE ABB=ON  PLU=ON  L184 AND L176
L186      16363 SEA FILE=EMBASE ABB=ON  PLU=ON  PHOTOCHEM?
L187          3 SEA FILE=EMBASE ABB=ON  PLU=ON  L185 AND L186
L188          8 SEA FILE=EMBASE ABB=ON  PLU=ON  L185 NOT L187


=> d que nos L210

L2              STR
L4            745 SEA FILE=REGISTRY FAM FUL L2
L6              STR
L8            387 SEA FILE=REGISTRY FAM FUL L6
L9              STR
L11         11383 SEA FILE=REGISTRY SSS FUL L9
L166     259655 SEA FILE=EMBASE ABB=ON  PLU=ON  IMMUNOSUPPRESSIVE AGENT+NT/CT
L167     600211 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENT+NT/CT
L169       7811 SEA FILE=EMBASE ABB=ON  PLU=ON  NICOTINIC ACID/CT
L170       4321 SEA FILE=EMBASE ABB=ON  PLU=ON  NICOTINAMIDE/CT
L171         35 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 AND EMBASE/LC
L172      14264 SEA FILE=EMBASE ABB=ON  PLU=ON  L171
L174      86419 SEA FILE=EMBASE ABB=ON  PLU=ON  ((L166 OR L167)) (L) AE/CT
L190       9076 SEA FILE=EMBASE ABB=ON  PLU=ON  L4
L191       4332 SEA FILE=EMBASE ABB=ON  PLU=ON  L8
L192       1271 SEA FILE=EMBASE ABB=ON  PLU=ON  (L190 OR L191) NOT (L170 OR
                  L169)
L193      15409 SEA FILE=EMBASE ABB=ON  PLU=ON  L172 OR L192
L194        333 SEA FILE=EMBASE ABB=ON  PLU=ON  L174 AND L193
L199      12130 SEA FILE=EMBASE ABB=ON  PLU=ON  ((ADVERSE OR UNDESIR? OR
                  INJUR? OR SIDE) (W) (AFFECT? OR EFFECT?))/TI
L200          3 SEA FILE=EMBASE ABB=ON  PLU=ON  L194 AND L199
L201      67201 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENT
L210          1 SEA FILE=EMBASE ABB=ON  PLU=ON  L200 AND L201


=> d que nos L211

L2              STR
```

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L4          745 SEA FILE=REGISTRY FAM FUL L2
L6              STR
L8          387 SEA FILE=REGISTRY FAM FUL L6
L9              STR
L11       11383 SEA FILE=REGISTRY SSS FUL L9
L166     259655 SEA FILE=EMBASE ABB=ON  PLU=ON  IMMUNOSUPPRESSIVE AGENT+NT/CT
L167     600211 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENT+NT/CT
L169       7811 SEA FILE=EMBASE ABB=ON  PLU=ON  NICOTINIC ACID/CT
L170       4321 SEA FILE=EMBASE ABB=ON  PLU=ON  NICOTINAMIDE/CT
L171         35 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 AND EMBASE/LC
L172      14264 SEA FILE=EMBASE ABB=ON  PLU=ON  L171
L174      86419 SEA FILE=EMBASE ABB=ON  PLU=ON  ((L166 OR L167)) (L) AE/CT
L176     149971 SEA FILE=EMBASE ABB=ON  PLU=ON  CHEMOTHERAPY+NT/CT
L178     120481 SEA FILE=EMBASE ABB=ON  PLU=ON  NEOPLAS?
L190       9076 SEA FILE=EMBASE ABB=ON  PLU=ON  L4
L191       4332 SEA FILE=EMBASE ABB=ON  PLU=ON  L8
L192       1271 SEA FILE=EMBASE ABB=ON  PLU=ON  (L190 OR L191) NOT (L170 OR
                L169)
L193      15409 SEA FILE=EMBASE ABB=ON  PLU=ON  L172 OR L192
L205      13019 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENT/CT (L)
                AE/CT
L207         19 SEA FILE=EMBASE ABB=ON  PLU=ON  L174 AND L193 AND L176 AND
                L205
L208     748982 SEA FILE=EMBASE ABB=ON  PLU=ON  ?TOXIC?
L209         15 SEA FILE=EMBASE ABB=ON  PLU=ON  L207 AND L208
L211          1 SEA FILE=EMBASE ABB=ON  PLU=ON  L209 AND L178


=> s (l188 or l210 or l211) not l165

L218         10 (L188 OR L210 OR L211) NOT L165

=> => dup rem L216 L217 L218
FILE 'CAPLUS' ENTERED AT 17:13:07 ON 26 OCT 2005
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PROCESSING COMPLETED FOR L216
PROCESSING COMPLETED FOR L217
PROCESSING COMPLETED FOR L218
L219         50 DUP REM L216 L217 L218 (1 DUPLICATE REMOVED)
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                ANSWERS '13-41' FROM FILE MEDLINE
                ANSWERS '42-50' FROM FILE EMBASE

=> d L219 ibib abs hitind hitstr 1-12; d iall 13-50 L219

L219 ANSWER 1 OF 50  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:1154561  CAPLUS
DOCUMENT NUMBER:          142:69221
TITLE:                    Nutraceutical for the prevention and treatment of
                          cancers and diseases affecting the liver
INVENTOR(S):              Bui, Can V.; Bui, Cuong Q.
PATENT ASSIGNEE(S):       USA
SOURCE:                   PCT Int. Appl., 42 pp.
```

previously printed with another search

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004112483	A1	20041229	WO 2004-US18380	20040610

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-478216P P 20030613

AB A composition comprising vegetable/herbal-based dietary ingredients, or exts., which contains vitamins and nutrients that provide a novel **nontoxic** treatment for liver cancers, hepatitis, and liver cirrhosis. The composition can be taken as a daily dietary supplement to enhance normal physiol. functions of the body. The said composition, or exts. thereof, are useful and effective in the treatment and prevention of liver and possibly other cancers. The compns. are also useful for administration to patients with pre-existing hepatitis and/or liver cirrhosis. The compns. or exts. thereof may be useful for treating other cancers and other disorders, diseases, or conditions.

IC ICM A01N065-00
ICS A61K035-78

CC 1-12 (Pharmacology)
Section cross-reference(s): 11, 18, 63

IT **Cytoprotective agents**
(hepatoprotective; nutraceutical for prevention and treatment of cancers and liver diseases)

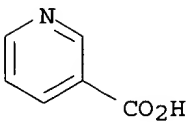
IT Antioxidants
Antitumor agents
Antiviral agents
Biliary tract, disease
Cirrhosis
Combination chemotherapy
Fruit and vegetable juices
Hepatitis
Hepatitis C virus
Honey
Human
Liver, disease
Liver, neoplasm
Neoplasm
Nutrition, animal
Prophylaxis
(nutraceutical for prevention and treatment of cancers and liver diseases)

IT 50-81-7, Vitamin C, biological studies 59-30-3, biological studies 59-43-8, Thiamin, biological studies **59-67-6**, Niacin, biological studies 83-88-5, Riboflavin, biological studies 120-72-9, Indole, biological studies 127-40-2, Lutein 144-68-3, Zeaxanthin 472-70-8,

Cryptoxanthin 502-65-8, Lycopene 1406-18-4, Vitamin E 7235-40-7, Beta carotene 7439-89-6, Iron, biological studies 7439-95-4, Magnesium, biological studies 7440-09-7, Potassium, biological studies 7440-23-5, Sodium, biological studies 7440-70-2, Calcium, biological studies 7723-14-0, Phosphorus, biological studies 7782-49-2, Selenium, biological studies 8059-24-3, Vitamin B6 11103-57-4, Vitamin A 12001-79-5, Vitamin K
RL: NPO (Natural product occurrence); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(nutraceutical for prevention and treatment of cancers and liver diseases)

IT **59-67-6**, Niacin, biological studies
RL: NPO (Natural product occurrence); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(nutraceutical for prevention and treatment of cancers and liver diseases)

RN 59-67-6 CAPLUS
CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L219 ANSWER 2 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:698116 CAPLUS
DOCUMENT NUMBER: 141:218937
TITLE: Histone deacetylase inhibitors of novel benzamide derivatives with potent differentiation and anti-proliferation activity
INVENTOR(S): Lu, Xian-ping; Li, Zhibin; Xie, Aihua; Li, Boyu; Ning, Zhiqiang; Shan, Song; Deng, Tuo; Hu, Weiming
PATENT ASSIGNEE(S): Shenzhen Chipscreen Biosciences Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071400	A2	20040826	WO 2004-IB401	20040209
WO 2004071400	A3	20050616		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,

BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004224991	A1	20041111	US 2004-770035		20040202
CA 2511479	AA	20040826	CA 2004-2511479		20040209
PRIORITY APPLN. INFO.:			US 2003-447915P	P	20030214
			US 2004-770035	A	20040202
			WO 2004-IB401	W	20040209

OTHER SOURCE(S): MARPAT 141:218937

AB The present invention is related to the preparation and pharmaceutical use of novel benzamide derivs. as histone deacetylase inhibitors (HDACI), their prepns. and the methods of using these compds. or their pharmaceutically acceptable salt in the treatment of cell proliferative diseases, e.g. cancer and psoriasis.

IC ICM A61K

CC 1-6 (Pharmacology)
Section cross-reference(s): 25, 27

IT Anti-inflammatory agents
Antitumor agents
Combination chemotherapy
Cytotoxic agents
Endocrine system, disease
Human
Immunomodulators
Inflammation
Neoplasm
Psoriasis
Transcription, genetic
(benzamide derivs. as histone deacetylase inhibitors with potent differentiation and anti-proliferation activity in relation to transcription activation of nuclear hormone receptors and combination with other agents)

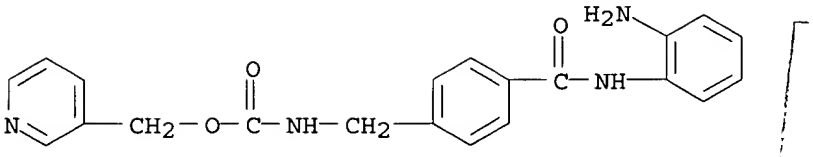
IT **Cytoprotective agents**
(neuroprotective; benzamide derivs. as histone deacetylase inhibitors with potent differentiation and anti-proliferation activity in relation to transcription activation of nuclear hormone receptors and combination with other agents)

IT **209783-80-2**, MS-275 503043-55-8
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(benzamide derivs. as histone deacetylase inhibitors with potent differentiation and anti-proliferation activity in relation to transcription activation of nuclear hormone receptors and combination with other agents)

IT **209783-80-2**, MS-275
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(benzamide derivs. as histone deacetylase inhibitors with potent differentiation and anti-proliferation activity in relation to transcription activation of nuclear hormone receptors and combination with other agents)

RN 209783-80-2 CAPLUS

CN Carbamic acid, [[4-[[(2-aminophenyl)amino]carbonyl]phenyl]methyl]-, 3-pyridinylmethyl ester (9CI) (CA INDEX NAME)



L219 ANSWER 3 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:677219 CAPLUS
DOCUMENT NUMBER: 142:189776
TITLE: Treatment of hyperlipidemia in cardiac transplant recipients
AUTHOR(S): Bilchick, Kenneth C.; Henrikson, Charles A.; Skojec, Diane; Kasper, Edward K.; Blumenthal, Roger S.
CORPORATE SOURCE: Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD, USA
SOURCE: American Heart Journal (2004), 148(2), 200-210
CODEN: AHJOA2; ISSN: 0002-8703
PUBLISHER: Elsevier, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Of the 60,000 patients receiving heart transplants between 1982 and 2001, approx. 12,000 are currently alive. The high incidence of hyperlipidemia and coronary disease (also known as accelerated graft atherosclerosis, or AGA) in these patients warrants early prophylaxis soon after transplantation with 3-hydroxy-3-methylglutaryl (HMG) Co-A reductase inhibitors (statins). Immunosuppressive agents such as prednisone, cyclosporine, mycophenylate mofetil, and sirolimus are associated with hyperlipidemia. Statins, in addition to lowering cholesterol levels, also benefit cardiac transplant recipients via effects on the immune system and endothelial function. Recent data have demonstrated that statins decrease AGA and mortality rates. Furthermore, greater benefits are seen when statins are started early. The 2 statins shown to decrease mortality in patients after cardiac transplantation are pravastatin and simvastatin, which differ in their metabolism (pravastatin is the only statin with non-cytochrome metabolism) and lipophilicity (pravastatin is less lipophilic). Although the benefit of simvastatin has been shown to extend to 8 yr after transplantation, increased adverse effects in other studies with higher doses of simvastatin have resulted in new prescribing recommendations, which state that the dose of simvastatin should probably not exceed 10 mg with cyclosporine or gemfibrozil and 20 mg with amiodarone or verapamil. The evidence for potential benefits, interactions, and adverse effects of other potential lipid-lowering drugs for this patient population, such as fibrates, niacin, fish oil, cholestyramine, and ezetimibe, are also discussed. A summary algorithm is proposed, including approaches to patients with statin-associated musculoskeletal symptoms and patients with inadequate results after initial statin therapy.

CC 1-0 (Pharmacology)
IT Fats and Glyceridic oils, biological studies
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fish; lipid-lowering drug fish oil, their potential benefits, interactions and **adverse effects** in treatment of hyperlipidemia in cardiac transplant recipient)
IT Drug toxicity
(high dose simvastatin showed long term survival of graft with major **adverse effects** in cardiac transplant patient undergoing hyperlipidemia treatment)

IT **Immunosuppressants**
Immunosuppression
(immunosuppressive agent, prednisone, cyclosporine, mycophenylate mofetil and sirolimus could be effectively used for hyperlipidemia treatment in cardiac transplant patient)

IT 163222-33-1, Ezetimibe
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-lowering drug ezetimibe, their potential benefits, interactions and **adverse effects** in treatment of hyperlipidemia in cardiac transplant recipient)

IT **59-67-6**, Niacin, biological studies
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lipid-lowering drug niacin, their potential benefits, interactions and **adverse effects** in treatment of hyperlipidemia in cardiac transplant recipient)

IT 11041-12-6, Cholestyramine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(review focuses on lipid-lowering drug cholestyramine, their potential benefits, interactions and **adverse effects** in treatment of hyperlipidemia in cardiac transplant recipient)

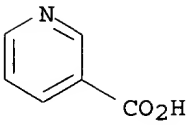
IT 1951-25-3, Amiodarone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simvastatin dose not exceeding 10 mg in combination with amiodarone could be effective in extending long term survival of graft without any major **adverse effects** in cardiac transplant patient under hyperlipidemia treatment)

IT 25812-30-0, Gemfibrozil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simvastatin dose not exceeding 10 mg in combination with gemfibrozil could be effective in extending long term survival of graft without any major **adverse effects** in cardiac transplant patient under hyperlipidemia treatment)

IT 52-53-9, Verapamil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simvastatin dose not exceeding 10 mg in combination with verapamil could be effective in extending long term survival of graft without any major **adverse effects** in cardiac transplant patient under hyperlipidemia treatment)

IT **59-67-6**, Niacin, biological studies
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lipid-lowering drug niacin, their potential benefits, interactions and **adverse effects** in treatment of hyperlipidemia in cardiac transplant recipient)

RN 59-67-6 CAPLUS
CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)



REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

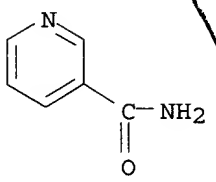
L219 ANSWER 4 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:796437 CAPLUS
DOCUMENT NUMBER: 139:271082
TITLE: L-Ergothioneine in neuroprotectant methods and compositions, and screening methods
INVENTOR(S): Aruoma, Okezie I.
PATENT ASSIGNEE(S): Oxis International, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082216	A2	20031009	WO 2003-US9840	20030328
WO 2003082216	A3	20040115		
WO 2003082216	C2	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480227	AA	20031009	CA 2003-2480227	20030328
EP 1496893	A2	20050119	EP 2003-723863	20030328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005521707	T2	20050721	JP 2003-579759	20030328
PRIORITY APPLN. INFO.:			US 2002-367845P P	20020328
			WO 2003-US9840 W	20030328

AB The invention provides methods for protecting a mammalian central nervous system cell from damage, as well as methods for treating or ameliorating neurodegenerative diseases. The invention also provides screening methods for neuroprotective agents that may alone, or in combination with other neuroprotective agents, aid in protecting cells of the central nervous system from damage attributed to **neurotoxic** compds., free radicals, or neurodegenerative diseases. The invention further provides pharmaceutical compns. comprising L-ergothioneine or other newly identified compds. and pharmaceutically acceptable carriers for administration to a mammal in need of neuroprotection.

IC ICM A61K
CC 1-11 (Pharmacology)
Section cross-reference(s): 63

IT **Cytoprotective agents**
(neuroprotective; ergothioneine in neuroprotectant methods and compns., and screening methods)
IT **Antitumor agents**
Nerve
Neurotoxicity
(**neurotoxic** compds.; ergothioneine in neuroprotectant methods and compns., and screening methods)
IT 50-81-7, Vitamin C, biological studies 70-18-8, Glutathione, biological studies 73-31-4, Melatonin **98-92-0**, Niacinamide 127-17-3, Pyruvic acid, biological studies 616-91-1, N-Acetylcysteine 1406-18-4, Vitamin E
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ergothioneine in neuroprotectant methods and compns., and screening methods)
IT 56-86-0, Glutamic acid, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**neurotoxic** compound; ergothioneine in neuroprotectant methods and compns., and screening methods)
IT 56-86-0D, Glutamic acid, analogs
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**neurotoxic** compds.; ergothioneine in neuroprotectant methods and compns., and screening methods)
IT **98-92-0**, Niacinamide
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ergothioneine in neuroprotectant methods and compns., and screening methods)
RN 98-92-0 CAPLUS
CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)



L219 ANSWER 5 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:319894 CAPLUS
DOCUMENT NUMBER: 138:337986
TITLE: Preparation of Lysocellin derivatives for prevention or alleviation of **side effect** of antitumor agents
INVENTOR(S): Fukasawa, Kazuteru; Sukenaga, Yoshikazu; Masuda, Akira; Yamada, Masatoshi; Masuda, Kuniko; Fujii, Hideji; Sakai, Toshiyuki; Nikaido, Toshio
PATENT ASSIGNEE(S): Nippon Kayaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003033491	A1	20030424	WO 2002-JP10676	20021015
W: CA, CN, KR, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
JP 2003128671	A2	20030508	JP 2001-318445	20011016
JP 2003128581	A2	20030508	JP 2001-327075	20011025
PRIORITY APPLN. INFO.:			JP 2001-318445 A	20011016
			JP 2001-327075 A	20011025

OTHER SOURCE(S): MARPAT 138:337986
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I and II [wherein X = H or (un)substituted aliphatic (cyclo)hydrocarbyl; Y = alkyl] and pharmaceutically acceptable salts thereof are prepared for prevention or alleviation of side effect of antitumor agents. For example, Lysocellin (NK34896A) was reacted with pivalic acid chloromethyl ester in DMF in the presence of DIEA to afford NK34896A pivaloyloxymethyl ester (III). Compound III showed IC50 of 0.11 μM against human cyclin A promotor activity.

IC ICM C07D407-14
ICS C07D493-04; C07D405-14; A61K031-341; A61K031-351; A61K031-4433; A61K045-00; A61P035-00; A61P043-00; C12P017-18; C12R001-465

CC 27-13 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST Lysocellin prevention alleviation **side effect** antitumor agent prepn; prevention alleviation **side effect** antitumor agent prepn NK34896A

IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A; preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

IT Bone marrow
(control; preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

IT **Antitumor agents**
Human
(preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

IT Hair
(unhairing; preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

IT 64889-60-7P 401947-65-7P, NK34896B 514847-26-8P 514847-27-9P 514847-28-0P 514847-30-4P 514847-31-5P 514847-32-6P 514847-33-7P 514847-34-8P 514847-35-9P **514847-36-0P** 514847-37-1P 514847-38-2P 514847-39-3P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

IT 33419-42-0, Etoposide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

IT 70-11-1, 2-Bromoacetophenone 75-03-6, Ethyl iodide 75-30-9,

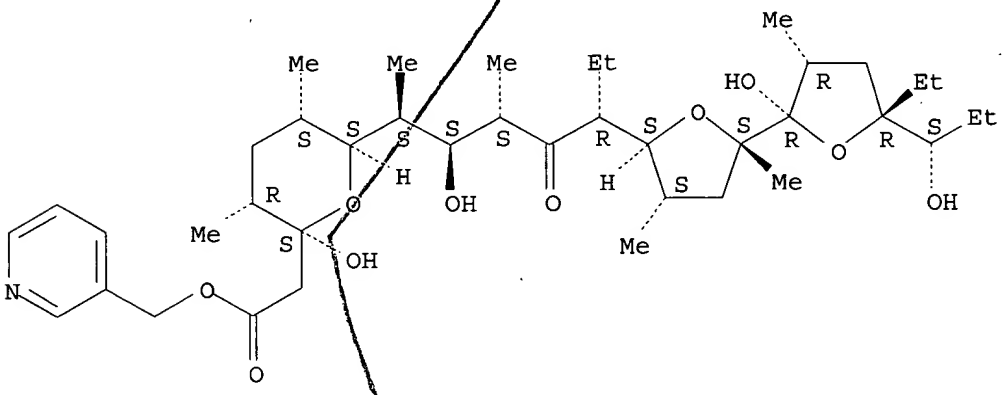
2-Iodopropane 100-44-7, Benzyl chloride, reactions 513-38-2, 1-Iodo-2-methylpropane 585-71-7, (1-Bromoethyl)benzene 615-83-8 3587-60-8, Benzyl chloromethyl ether 5292-43-3 6959-48-4 18107-18-1, Trimethylsilyldiazomethane 18997-19-8, Pivalic acid chloromethyl ester 55898-33-4, Lysocellin
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

IT **514847-36-0P**
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of Lysocellin esters for prevention or alleviation of **side effect** of antitumor agents)

RN 514847-36-0 CAPLUS

CN 2H-Pyran-2-acetic acid, 6-[(1S,2S,3S,5R)-5-[(2S,2'R,3'R,4S,5S,5'R)-5'-ethyloctahydro-2'-hydroxy-5'-[(1S)-1-hydroxypropyl]-2,3',4-trimethyl[2,2'-bifuran]-5-yl]-2-hydroxy-1,3-dimethyl-4-oxoheptyl]tetrahydro-2-hydroxy-3,5-dimethyl-, 3-pyridinylmethyl ester, (2S,3R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L219 ANSWER 6 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:748278 CAPLUS
DOCUMENT NUMBER: 140:280869
TITLE: Effect of taurine and other antioxidants on the growth of colon carcinoma cells in the presence of doxorubicin or vinblastine in hypoxic or in ambient oxygen conditions: effect of antioxidants on the action of antineoplastic drugs in MDR and non-MDR cells
AUTHOR(S): Wersinger, C.; Rebel, G.; Lelong-Rebel, I.
CORPORATE SOURCE: UPR 9003 du CNRS, Institut de Recherche Contre les Cancers de l'Appareil Digestif, Hopitaux Universitaires, Strasbourg, F 67091, Fr.
SOURCE: Advances in Experimental Medicine and Biology (2003), 526(Taurine 5), 411-417
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three LoVo cell lines, derived from a supraclavicular metastasis of human colon carcinoma were used to study the effects of taurine and other antioxidants on doxorubicin or vinblastine-induced inhibition of cell proliferation in hypoxic or ambient conditions. The three cell lines studied include LoVo-Dox, LoVo-f (LoVo-S fusoid), and LoVo-s.c. (LoVo-S small cells). Growth of the three LoVo cell lines was notably reduced when cultured in a hypoxic environment instead of in air: 5% CO2 (20% O2). This growth reduction was less significant for the chemoresistant LoVo-Dox cells than for the two chemosensitive-f and -s.c. variants. The growth of the two sensitive lines in the presence of doxorubicin was affected much more when cultured in 20% O2 than in hypoxic medium. Doxorubicin was found to be a potent inhibitor of growth of the three cell lines, which was not modified by taurine, carnitine, niacin or N-acetylcysteine. Trolox reversed the cytotoxicity of the anthracyclines, the effect nearly complete under hypoxic conditions. Vinblastine also inhibited LoVo cell growth. Taurine, trolox, carnitine, niacin, and N-acetylserine had no effect on vinblastine cytotoxicity.

CC 1-6 (Pharmacology)

IT Drug interactions
(**adverse; effect** of taurine and other antioxidants on the growth of colon carcinoma cells in the presence of doxorubicin or vinblastine in hypoxic or in ambient oxygen conditions)

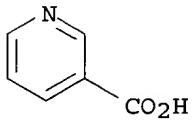
IT **Antitumor agents**
(colon carcinoma; effect of taurine and other antioxidants on the growth of colon carcinoma cells in the presence of doxorubicin or vinblastine in hypoxic or in ambient oxygen conditions)

IT **59-67-6**, Niacin, biological studies 107-35-7, Taurine 541-15-1, Carnitine 865-21-4, Vinblastine 16354-58-8, N-Acetylserine 23214-92-8, Doxorubicin 53188-07-1, Trolox
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effect of taurine and other antioxidants on the growth of colon carcinoma cells in the presence of doxorubicin or vinblastine in hypoxic or in ambient oxygen conditions)

IT **59-67-6**, Niacin, biological studies
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effect of taurine and other antioxidants on the growth of colon carcinoma cells in the presence of doxorubicin or vinblastine in hypoxic or in ambient oxygen conditions)

RN 59-67-6 CAPLUS

CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

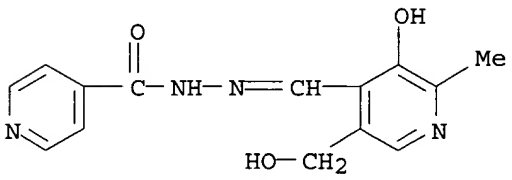
L219 ANSWER 7 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:654559 CAPLUS
DOCUMENT NUMBER: 140:246252
TITLE: Prevention of anthracycline type antibiotic **toxicity** using new Fe-chelating agents
AUTHOR(S): Schroeterova, Ladislava; Kvasnickova, Eva; Gersl,

Vladimir
CORPORATE SOURCE: Department of Biochemical Sciences, Faculty of Pharmacy, Charles University in Prague, Hradec Kralove, Czech Rep.
SOURCE: Folia Pharmaceutica Universitatis Carolinae (2003), 27-28, 77-83
CODEN: FUPCEA; ISSN: 1210-9495
PUBLISHER: Karolinum - Charles University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exptl. conditions were optimized for the study of the in vitro and in vivo cardioprotective effects of the new lipophilic iron chelates, pyridoxal isonicotinoyl hydrazone (PIH) and salicylaldehyde isonicotinyl hydrazone (SIH) on the activity of enzymes involved in the metabolism of anthracyclines. Two non-specific aniline- and amidopyrine-dependent microsomal P 450 monooxygenases were used to establish the conditions for proper tissue sampling, storage and handling conditions. The conditions were further verified by assaying the samples for the activities of P 450 isoenzymes, which play an important role in the metabolism of anthracyclines, biotransformation of other drugs or pollutants entering the body from the environment.
CC 1-6 (Pharmacology)
ST anthracycline biotransformation iron chelating agent **cardiotoxicity** cardioprotection
IT Antibiotics
(anthracycline; prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)
IT Heart, disease
(cardiomyopathy; prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)
IT **Cytoprotective agents**
(cardioprotective; prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)
IT **Antitumor agents**
Chelating agents
Heart
Neoplasm
(prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)
IT 23214-92-8, Doxorubicin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)
IT 7439-89-6, Iron, biological studies 9035-51-2, Cytochrome P 450, biological studies 9039-06-9, NADPH-cytochrome P450 reductase 59793-97-4, 7-Ethoxyresorufin O-dealkylase 83682-88-6, 7-Methoxyresorufin O-dealkylase 85204-91-7, 7-Benzyloxyresorufin O-dealkylase 96595-04-9, 7-Pentoxyresorufin O-dealkylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)
IT 495-84-1 **737-86-0**, Pyridoxal isonicotinoyl hydrazone
RL: **DMA (Drug mechanism of action); PAC (Pharmacological**

activity); **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)

IT **737-86-0**, Pyridoxal isonicotinoyl hydrazone
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(prevention of antitumor anthracycline type antibiotic **cardiotoxicity** using new Fe-chelating agents and assaying of P 450 isoenzymes)

RN 737-86-0 CAPLUS
CN 4-Pyridinecarboxylic acid, [[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridinyl]methylene]hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L219 ANSWER 8 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:172400 CAPLUS
DOCUMENT NUMBER: 136:210557
TITLE: Method using a cytoprotectant for reducing dermal **toxicity** of a **cytotoxic** agent
INVENTOR(S): Colbern, Gail T.; Steinmetz, Karen; Working, Peter K.; Gabizon, Alberto A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002028237	A1	20020307	US 2001-839918		20010420
PRIORITY APPLN. INFO.:			US 2000-199012P	P	20000420

AB Methods are provided for reducing the incidence and occurrence of dermal lesions in mammals, particularly human patients, who receive chemotherapy treatment and in the course of such treatment are administered liposomal formulations of **cytotoxic** agents. **Cytotoxic** agents typically include doxorubicin, cytarabine, epirubicin, daunorubicin, 5-fluorouracil (5-FU) and vinorelbine. Reduction in the incidence and occurrence of dermal lesions in a patient is achieved by administration of a cytoprotective agent, e.g. amifostine.

IC ICM A61K009-127
ICS A61K031-7068; A61K031-704; A61K031-513; A61K031-48
INCL 424450000
CC 1-6 (Pharmacology)
ST dermal **cytotoxicity** **cytotoxic** agent cytoprotectant;

amifostine cytoprotectant dermal **cytotoxicity cytotoxic** agent

IT Intestine, neoplasm
(colon, inhibitors; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT **Antitumor agents**
(colon; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT **Antitumor agents**
Chemotherapy
Cytoprotective agents
Cytotoxic agents
Drug interactions
Skin, disease
(cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT Lung, neoplasm
(inhibitors; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT Drug delivery systems
(liposomes; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT **Antitumor agents**
(lung; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT **Antitumor agents**
(lymphoma; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT Drug interactions
(pharmacokinetic; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT Skin, disease
(plantar-planar erythrodysesthesia; cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

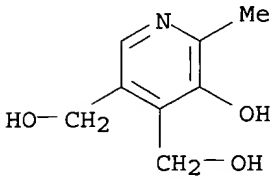
IT 23214-92-8, Doxorubicin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT 51-21-8, 5-Fluorouracil 147-94-4, Cytarabine 20830-81-3, Daunorubicin 56420-45-2, Epirubicin 71486-22-1, Vinorelbine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT **65-23-6**, Pyridoxine 113-15-5, Ergotamine 20537-88-6, Amifostine
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**cytoprotectant** for reducing dermal **toxicity** of **cytotoxic** agent)

IT 25322-68-3, Polyethylene glycol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytoprotectant for reducing dermal **toxicity** of **cytotoxic** agent)

IT **65-23-6**, Pyridoxine
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**cytoprotectant** for reducing dermal **toxicity** of **cytotoxic** agent)
RN 65-23-6 CAPLUS
CN 3,4-Pyridinedimethanol, 5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)



L219 ANSWER 9 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:464048 CAPLUS
DOCUMENT NUMBER: 131:82989
TITLE: Nitric oxide-releasing chelating agents and their therapeutic use
INVENTOR(S): Towart, Robertson; Karlsson, Jan Olof Gustav; Wistrand, Lars Goran; Malmgren, Hakan
PATENT ASSIGNEE(S): Nycomed Imaging A/S, Norway
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933823	A1	19990708	WO 1998-GB3840	19981218
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9917702	A1	19990719	AU 1999-17702	19981218
EP 1060174	A1	20001220	EP 1998-962567	19981218
EP 1060174	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001527072	T2	20011225	JP 2000-526505	19981218
AT 277038	E	20041015	AT 1998-962567	19981218
ZA 9811825	A	19990708	ZA 1998-11825	19981223
US 6391895	B1	20020521	US 2000-599862	20000623

PRIORITY APPLN. INFO.:
GB 1997-27226 A 19971223
US 1998-76793P P 19980304
GB 1998-5450 A 19980313
WO 1998-GB3840 W 19981218

OTHER SOURCE(S): MARPAT 131:82989
AB Chelating agents, in particular dipyridoxyl and aminopolycarboxylic

acid-based chelating agents, and their metal chelates, when linked directly or indirectly to at least one nitric oxide-releasing moiety, or when use in combination with nitric oxide or a nitric oxide-releasing moiety, have been found to be effective in treating a variety of disorders. In particular, such compds. may be used in treating conditions associated with the presence of free radicals in the body, e.g. reperfusion injuries, and in reducing the **cardiotoxicity** of anti-tumor agents, e.g. anthracyclines and/or paclitaxel.

IC C07D401-12; A61K031-44

CC 1-12 (Pharmacology)
Section cross-reference(s): 63

ST nitric oxide releasing chelating agent therapeutic; dipyridoxyl chelating agent NO releasing therapeutic; aminopolycarboxylate chelating agent NO releasing therapeutic; radical disease NO releasing chelating agent; reperfusion injury NO releasing chelating agent; antitumor **cardiotoxicity** NO releasing chelating agent; anthracycline antitumor **cardiotoxicity** NO releasing chelating agent; paclitaxel **cardiotoxicity** NO releasing chelating agent

IT Anthracyclines
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor, **cardiotoxicity** from; nitric oxide-releasing chelating agents, and therapeutic use)

IT **Cytoprotective agents**
(cardioprotective; nitric oxide-releasing chelating agents, and therapeutic use)

IT **Antitumor agents**
(**cardiotoxicity** reduction; nitric oxide-releasing chelating agents, and therapeutic use)

IT **Toxicity**
(**cardiotoxicity**, of antitumor agents; nitric oxide-releasing chelating agents, and therapeutic use)

IT 20830-81-3, Daunomycin 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cardiotoxicity** from; nitric oxide-releasing chelating agents, and therapeutic use)

IT 55-63-0D, Nitroglycerine, chelating agent conjugates 67-45-8D, Furoxane, derivs., chelating agent conjugates 74-79-3D, L-Arginine, chelating agent conjugates, biological studies 78-11-5D, Pentaerythritol tetranitrate, chelating agent conjugates 87-33-2D, Isosorbide dinitrate, chelating agent conjugates 110-46-3D, Isoamyl nitrite, chelating agent conjugates 463-04-7D, Amyl nitrite, chelating agent conjugates 542-56-3D, Isobutyl nitrite, chelating agent conjugates 7297-25-8D, Erythritol tetranitrate, chelating agent conjugates 7803-49-8D, Hydroxylamine, chelating agent conjugates, biological studies 13755-38-9 14402-89-2D, Sodium nitroprusside, chelating agent conjugates 14452-93-8D, Nitrosonium, salts, chelating agent conjugates 14854-54-7 16051-77-7D, Isosorbide mononitrate, chelating agent conjugates 18550-55-5D, Hyponitric acid, chelating agent conjugates 18883-66-4D, Streptozotocin, chelating agent conjugates 19059-14-4D, Peroxynitrite, chelating agent conjugates 25717-80-0D, Molsidomine, chelating agent conjugates 33876-97-0D, SIN-1, chelating agent conjugates 51209-75-7D, S-Nitrosocysteine, chelating agent conjugates 57564-91-7D, SNOG, chelating agent conjugates 62502-74-3D, chelating agent conjugates 67776-06-1D, SNAP, chelating agent conjugates 69078-52-0D, derivs., chelating agent conjugates 79032-48-7D, S-Nitroso-N-acetylpenicillamine, chelating agent conjugates **88969-06-6D**, PLED, conjugates with

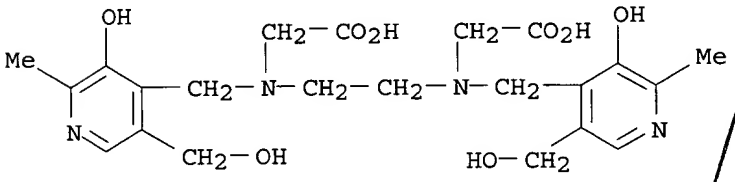
nitric oxide-releasing moieties **118248-91-2D**, DPDP, conjugates with nitric oxide-releasing moieties 130432-17-6D, SPM 3672, chelating agent conjugates 132722-74-8D, Pirsidomine, chelating agent conjugates 136587-13-8D, chelating agent conjugates 138472-01-2D, NOR 3, chelating agent conjugates 139146-66-0D, SPM 5185, chelating agent conjugates 144575-52-0D, GEA 5024, chelating agent conjugates 144576-10-3D, GEA 3162, chelating agent conjugates 146724-84-7D, NOC-7, chelating agent conjugates 146724-94-9D, Deta-no, chelating agent conjugates 164301-47-7D, GEA 5583, chelating agent conjugates 170637-67-9D, chelating agent conjugates 173903-12-3D, chelating agent conjugates 174175-11-2D, NOR 1, chelating agent conjugates 199666-24-5D, NOC-5, chelating agent conjugates 199666-29-0 199666-32-5D, chelating agent conjugates 230302-19-9D, chelating agent conjugates 230302-20-2D, glyco derivs., chelating agent conjugates **230302-21-3D**, conjugates with nitric oxide-releasing moieties **230302-22-4D**, conjugates with nitric oxide-releasing moieties **230309-88-3D**, DPMP, conjugates with nitric oxide-releasing moieties
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nitric oxide-releasing chelating agents, and therapeutic use)

IT 7429-91-6D, Dysprosium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7439-89-6D, Iron, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7439-95-4D, Magnesium, DPDP complexes, NO-releasing moiety conjugates, biological studies 7439-96-5D, Manganese, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7439-98-7D, Molybdenum, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-00-8D, Neodymium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-02-0D, Nickel, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-10-0D, Praseodymium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-12-2D, Promethium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-18-8D, Ruthenium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-19-9D, Samarium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-27-9D, Terbium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-30-4D, Thulium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-32-6D, Titanium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-45-1D, Cerium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-47-3D, Chromium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-48-4D, Cobalt, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-50-8D, Copper, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-52-0D, Erbium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-53-1D, Europium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-54-2D, Gadolinium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-55-3D, Gallium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-60-0D, Holmium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-62-2D, Vanadium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-64-4D, Ytterbium, chelates with chelating agent-NO-releasing moiety conjugates, biological studies 7440-66-6D, Zinc, chelates with chelating agent-NO-releasing moiety conjugates, biological studies

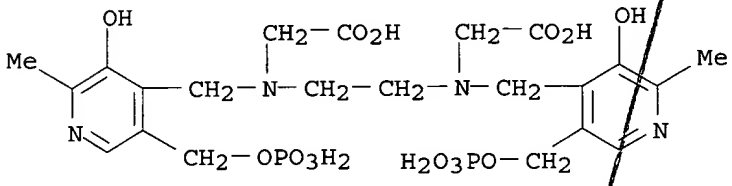
118248-91-2D, alkali and alkaline earth metal complexes, NO-releasing moiety conjugates **201539-62-0D**, NO-releasing moiety conjugates **230302-23-5D**, NO-releasing moiety conjugates
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nitric oxide-releasing chelating agents, chelates, and therapeutic use)

IT **88969-06-6D**, PLED, conjugates with nitric oxide-releasing moieties **118248-91-2D**, DPDP, conjugates with nitric oxide-releasing moieties **230302-21-3D**, conjugates with nitric oxide-releasing moieties **230302-22-4D**, conjugates with nitric oxide-releasing moieties **230309-88-3D**, DPMP, conjugates with nitric oxide-releasing moieties
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nitric oxide-releasing chelating agents, and therapeutic use)

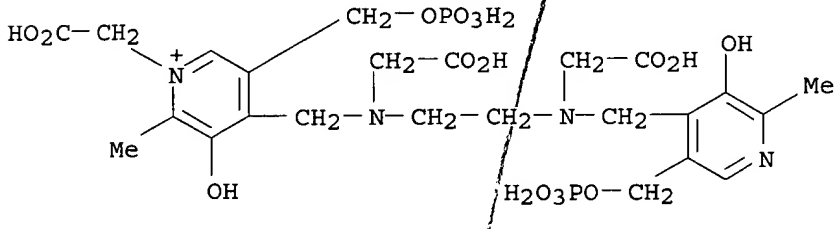
RN 88969-06-6 CAPLUS
CN Glycine, N,N'-1,2-ethanediylbis[N-[[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)



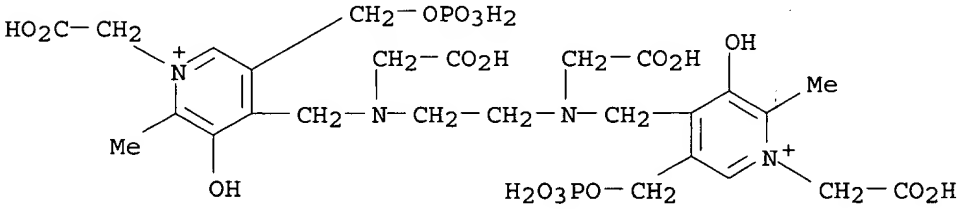
RN 118248-91-2 CAPLUS
CN Glycine, N,N'-1,2-ethanediylbis[N-[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)



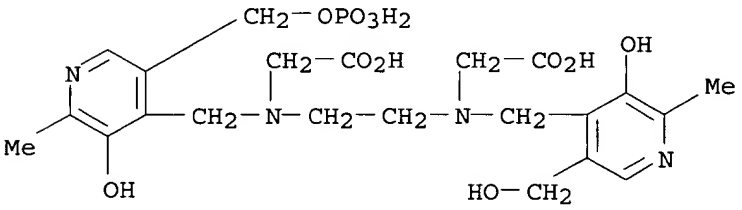
RN 230302-21-3 CAPLUS
CN Pyridinium, 1-(carboxymethyl)-4-[[(carboxymethyl)[2-[(carboxymethyl)[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]amino]ethyl]amino]methyl]-3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)



RN 230302-22-4 CAPLUS
CN Pyridinium, 4,4'-[1,2-ethanediylbis[[(carboxymethyl)imino]methylene]]bis[1-(carboxymethyl)-3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)

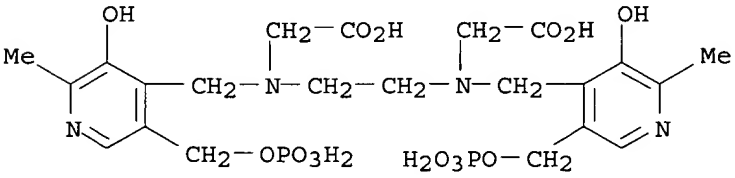


RN 230309-88-3 CAPLUS
CN Glycine, N-[2-[(carboxymethyl)[[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridinyl]methyl]amino]ethyl]-N-[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

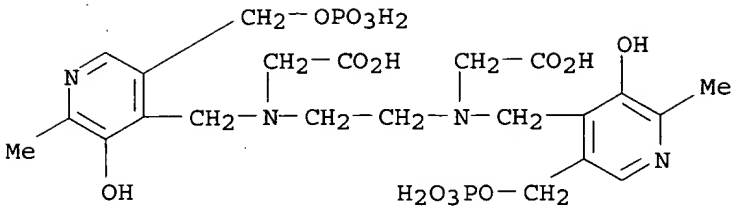


IT **118248-91-2D**, alkali and alkaline earth metal complexes, NO-releasing moiety conjugates **201539-62-0D**, NO-releasing moiety conjugates **230302-23-5D**, NO-releasing moiety conjugates
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nitric oxide-releasing chelating agents; chelates, and therapeutic use)

RN 118248-91-2 CAPLUS
CN Glycine, N,N'-1,2-ethanediylbis[N-[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

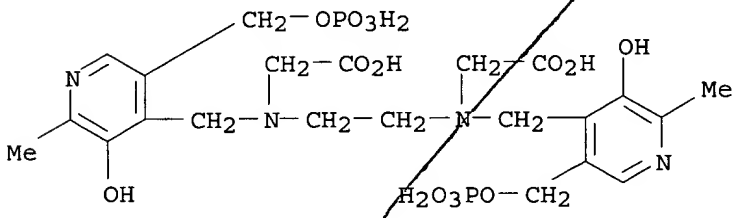


RN 201539-62-0 CAPLUS
CN Glycine, N,N'-1,2-ethanediylbis[N-[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]-, sodium salt (9CI) (CA INDEX NAME)



● x Na

RN 230302-23-5 CAPLUS
CN Glycine, N,N'-1,2-ethanediylbis[N-[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]-, calcium salt (9CI) (CA INDEX NAME)



● x Ca

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

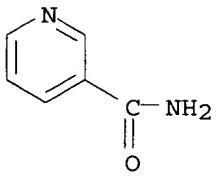
L219 ANSWER 10 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:6829 CAPLUS
DOCUMENT NUMBER: 132:290541
TITLE: Complex protection and repair (therapy) of urethane- and radiation-induced chromosomal lesions and carcinogenesis
AUTHOR(S): Kraskovskii, G. V.; Mironova, G. I.; Gorobets, L. V.; Dosetskaya, S. D.; Fedorova, M. V.
CORPORATE SOURCE: Inst. Fiziol., NAN Belarusi, Belarus
SOURCE: Doklady Natsional'noi Akademii Nauk Belarusi (1999), 43(3), 85-88
CODEN: DNABFW; ISSN: 1561-8323
PUBLISHER: Belaruskaya Navuka
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Nicotinamide (1% 0.6 mL) radioprotective, cytoprotective, and carcinogenesis inhibiting properties were tested in mice administered urethane (1.5 mg/g) and thymaline or irradiated by roentgen rays.
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 1
IT **Antitumor agents**
Bone marrow

Chromosome aberrations
Cytoprotective agents
Radioprotectants
(nicotinamide radioprotectant and cytoprotectant properties)

IT **98-92-0**, Nicotinamide
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nicotinamide radioprotectant and **cytoprotectant** properties)

IT **98-92-0**, Nicotinamide
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nicotinamide radioprotectant and **cytoprotectant** properties)

RN 98-92-0 CAPLUS
CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)



L219 ANSWER 11 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:42269 CAPLUS
DOCUMENT NUMBER: 128:84398
TITLE: Reduction of **cardiotoxicity** of an antitumor agent using chelating agents or chelates, particularly manganese chelates
INVENTOR(S): Towart, Robertson; Karlsson, Jan Olof Gustav; Jynge, Per
PATENT ASSIGNEE(S): Nycomed Imaging AS, Norway; Towart, Robertson; Karlsson, Jan Olof Gustav; Jynge, Per
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9749390	A1	19971231	WO 1997-GB1721	19970624
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2258299	AA	19971231	CA 1997-2258299	19970624
CA 2259150	AA	19971231	CA 1997-2259150	19970624
AU 9732688	A1	19980114	AU 1997-32688	19970624
AU 720570	B2	20000608		
EP 910360	A1	19990428	EP 1997-928368	19970624

EP 910360	B1	20021127			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1228694	A	19990915	CN 1997-197429		19970624
CN 1228703	A	19990915	CN 1997-197438		19970624
NZ 333357	A	20000825	NZ 1997-333357		19970624
JP 2000514044	T2	20001024	JP 1998-502557		19970624
AT 228361	E	20021215	AT 1997-928368		19970624
NO 9805917	A	19990125	NO 1998-5917		19981217
US 6147094	A	20001114	US 1998-213246		19981217
PRIORITY APPLN. INFO.:			GB 1996-13182	A	19960624
			WO 1997-GB1721	W	19970624

OTHER SOURCE(S): MARPAT 128:84398

AB The invention relates to the use of certain chelating agents and their metal chelates and to the use of certain manganese containing compds., in particular manganese chelates, in the manufacture of a therapeutic agent for use in reducing the **cardiotoxicity** of an antitumor agent. Such compds. are particularly effective in reducing the side-effects of anthracycline drugs and/or paclitaxel.

IC ICM A61K031-195
ICS A61K031-28; A61K031-675; A61K033-32; A61K031-44; A61K031-195; A61K031-00; A61K031-28; A61K031-00; A61K031-675; A61K031-00; A61K033-32; A61K031-00; A61K031-44; A61K031-00

CC 1-8 (Pharmacology)
Section cross-reference(s): 63

ST antitumor agent **cardiotoxicity** redn manganese chelate; chelating agent chelate antitumor agent **cardiotoxicity**; anthracycline paclitaxel antitumor **cardiotoxicity** manganese chelate

IT **Antitumor agents**
Drug delivery systems
(antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

IT Anthracyclines
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

IT **Cytoprotective agents**
(cardioprotective; antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

IT **Toxicity**
(**cardiotoxicity**; antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

IT Alkali metal compounds
Alkaline earth metals
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chelates; antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

IT Heart
(**toxicity**; antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

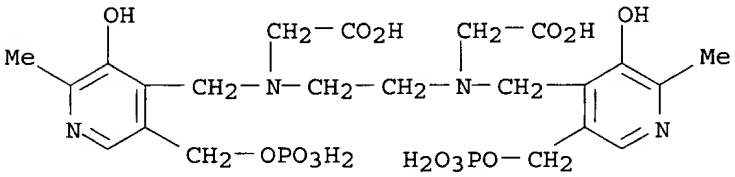
IT 20830-81-3, Daunomycin 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agent **cardiotoxicity** reduction with chelating agents

or chelates, particularly manganese chelates)

IT 60-00-4, Ethylenediaminetetraacetic acid, biological studies 67-43-6, Diethylenetriaminepentaacetic acid 7429-91-6D, Dysprosium, chelates, biological studies 7439-89-6D, Iron, chelates, biological studies 7439-95-4D, Magnesium, chelates, biological studies 7439-96-5D, Manganese, chelates, biological studies 7439-98-7D, Molybdenum, chelates, biological studies 7440-00-8D, Neodymium, chelates, biological studies 7440-02-0D, Nickel, chelates, biological studies 7440-10-0D, Praseodymium, chelates, biological studies 7440-12-2D, Promethium, chelates, biological studies 7440-18-8D, Ruthenium, chelates, biological studies 7440-19-9D, Samarium, chelates, biological studies 7440-23-5D, Sodium, chelates, biological studies 7440-27-9D, Terbium, chelates, biological studies 7440-30-4D, Thulium, chelates, biological studies 7440-32-6D, Titanium, chelates, biological studies 7440-45-1D, Cerium, chelates, biological studies 7440-47-3D, Chromium, chelates, biological studies 7440-48-4D, Cobalt, chelates, biological studies 7440-50-8D, Copper, chelates, biological studies 7440-52-0D, Erbium, chelates, biological studies 7440-53-1D, Europium, chelates, biological studies 7440-54-2D, Gadolinium, chelates, biological studies 7440-55-3D, Gallium, chelates, biological studies 7440-60-0D, Holmium, chelates, biological studies 7440-62-2D, Vanadium, chelates, biological studies 7440-64-4D, Ytterbium, chelates, biological studies 7440-66-6D, Zinc, chelates, biological studies 7440-70-2D, Calcium, chelates, biological studies 7773-01-5, Manganese chloride 55448-20-9 56731-38-5 **118248-91-2** 118248-93-4 118248-95-6 126217-20-7 201042-24-2
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

IT **118248-91-2**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antitumor agent **cardiotoxicity** reduction with chelating agents or chelates, particularly manganese chelates)

RN 118248-91-2 CAPLUS
CN Glycine, N,N'-1,2-ethanediylbis[N-[[3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)



L219 ANSWER 12 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:622997 CAPLUS
DOCUMENT NUMBER: 127:229654
TITLE: Methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species
INVENTOR(S): Bredesen, Dale E.; Kane, Darcie J.
PATENT ASSIGNEE(S): Regents of the University of California, USA; Bredesen, Dale E.; Kane, Darcie J.

SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733473	A1	19970918	WO 1997-US4038	19970314
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6231852	B1	20010515	US 1996-707055	19960903
AU 9720792	A1	19971001	AU 1997-20792	19970314
PRIORITY APPLN. INFO.:			US 1996-616604 A	19960315
			US 1996-707055 A1	19960903
			US 1993-154281 B1	19931118
			WO 1997-US4038 W	19970314

AB Methods are provided for controlling cell death when the cell is exposed to one or more potentially lethal cellular insults. In one method, cell death is inhibited by introducing a reactive oxygen species limiter into the cell which prevents the build up of lethal levels of reactive oxygen species when the cell is exposed to a cellular insult. In another method, cell death is promoted in cancer cells or other proliferating cells which are naturally resistant to lethal cellular insults. The method involves neutralizing reactive oxygen species limiters, such as bcl-2, which occur naturally in cancer cells and which prevent the build up of reactive oxygen species within the cancer cells when they are exposed to lethal cellular insult. Neutralizing the reactive oxygen species limiter leaves the cancer cell unable to protect itself when cellular insult causes increases in the level of reactive oxygen species. The result is an increase in cell death.

IC ICM A01N039-00
ICS A01N037-18; A61K038-00; A61K033-40; A61K039-00; C12N005-00

CC 1-6 (Pharmacology)

IT **Antitumor agents**
Antitumor agents
(B-cell lymphoma; methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

IT **Antitumor agents**
(carcinoma, heart carcinoma; methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

IT **Chemotherapy**
(cell proliferation treatment with chemotherapeutic agent and neutralizing agent for reactive oxygen species limiter)

IT **Antitumor agents**
(lung small-cell carcinoma; methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

IT **Antitumor agents**
Apoptosis
Cell death

Cell nucleus
Cytoprotective agents
Oxidative phosphorylation, biological
Oxidative stress, biological
(methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

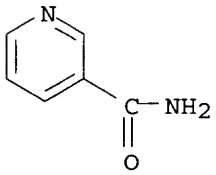
IT **Antitumor agents**
(neuroblastoma; methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

IT **Antitumor agents**
(prostate gland; methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

IT 50-81-7, L-Ascorbic acid, biological studies 58-27-5, Menadione 61-82-5, 1H-1,2,4-Triazol-3-amine 67-42-5, EGTA 74-31-7, N,N'-Diphenyl-p-phenylenediamine 75-91-2, tert-Butyl hydroperoxide **98-92-0**, Nicotinamide 5072-26-4, Buthionine sulfoximine 50903-99-6, L-NAME 52665-69-7, A23187 56092-81-0, Ionomycin 79032-48-7, S-Nitroso-N-acetylpenicillamine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

IT **98-92-0**, Nicotinamide
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(methods for reducing bcl-2-expressing cells resistance to death and for controlling cell death by controlling production of reactive oxygen species)

RN 98-92-0 CAPLUS
CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)



L219 ANSWER 13 OF 50 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004352338 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15255289
TITLE: A combination therapy with copper nicotinate complex reduces the adverse effects of 5-fluorouracil on patients with hepatocellular carcinoma.
AUTHOR: El-Saadani Muhammad A M
CORPORATE SOURCE: Department of Biochemistry, Faculty of Science, Alexandria University, Egypt.. el_saadaniM@hotmail.com
SOURCE: Journal of experimental therapeutics & oncology, (2004 Apr) 4 (1) 19-24.
Journal code: 9604933. ISSN: 1359-4117.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040717
Last Updated on STN: 20040806
Entered Medline: 20040805

ABSTRACT:
5-Fluorouracil (5-FU) as chemotherapy in cases of hepatocellular carcinoma (HCC), was found to initiate **hepatotoxic** injuries, ascites, leucopenia, thrombocytopenia and myelosupression that limit its use. Therefore, this work was conducted to investigate whether the combination of copper (I)-nicotinate complex [CuCl (HNA)2] with 5-FU may overcome such a drug resistance. Forty-eight patients with HCC were therapy-naive and treated with 5-FU (12 mg/kg/day) for 5 days in 2 cycles with 4 weeks in between. Twenty-four of them were simultaneously given oral doses of copper (I)-nicotinate complex (0.8 mg/kg/day) started with the 5-FU treatment. The combined therapy of CuCl (HNA)2 with 5-FU could improve the prognosis of HCC-patients. Improvement of liver function was presented by significant reduction of serum bilirubin ($p<0.001$), transaminases and alkaline phoshatase ($p<0.05$). The copper complex prevented hypoproteinaemic and hypoalbuminaemic effects of 5-FU and rendered the prothrombin time to its normal value ($p<0.001$). Superoxide dismutase, ceruloplasmin and immunoglobulins IgG showed significant increases ($p<0.001$), while serum copper and lipid peroxides were reduced ($p<0.001$). Thrombocytopenia, leucopenia and other myelosuppressive effects of 5-FU were reduced by the co-administration of CuCl (HNA)2. In conclusion the combination with CuCl (HNA)2 given in such a dosage schedule mitigated the most frequent **toxicities** associating 5-FU administration and enhanced defense mechanisms against oxidative stress.

CONTROLLED TERM: Check Tags: Male
Alkaline Phosphatase: BL, blood
Antimetabolites, Antineoplastic: AE, adverse effects
*Antimetabolites, Antineoplastic: TU, therapeutic use
Bilirubin: BL, blood
*Carcinoma, Hepatocellular: DT, drug therapy
Carcinoma, Hepatocellular: PA, pathology
Ceruloplasmin: ME, metabolism
*Copper: TU, therapeutic use
Drug Combinations
Fluorouracil: AE, adverse effects
*Fluorouracil: TU, therapeutic use
Humans
Hypoalbuminemia: DT, drug therapy
Hypoalbuminemia: ET, etiology
Hypoproteinemia: DT, drug therapy
Hypoproteinemia: ET, etiology
Immunoglobulin G: ME, metabolism
Liver Function Tests
*Liver Neoplasms: DT, drug therapy
Liver Neoplasms: PA, pathology
Niacin: AE, adverse effects
***Niacin: TU, therapeutic use**
Prognosis
Superoxide Dismutase: ME, metabolism
Transaminases: BL, blood

CAS REGISTRY NO.: 51-21-8 (Fluorouracil); 59-67-6 (Niacin); 635-65-4 (Bilirubin); 7440-50-8 (Copper)
CHEMICAL NAME: 0 (Antimetabolites, Antineoplastic); 0 (Drug Combinations);

0 (Immunoglobulin G); EC 1.15.1.1 (Superoxide Dismutase); EC 1.16.3.1 (Ceruloplasmin); EC 2.6.1. (Transaminases); EC 3.1.3.1 (Alkaline Phosphatase)

L219 ANSWER 14 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2005203888 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15838404
TITLE: Treatment of vincristine-induced cranial polyneuropathy.
AUTHOR: Duman Ozgur; Tezcan Gulsun; Hazar Volkan
SOURCE: Journal of pediatric hematology/oncology : official journal of the American Society of Pediatric Hematology/Oncology, (2005 Apr) 27 (4) 241-2.
Journal code: 9505928. ISSN: 1077-4114.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050420
Last Updated on STN: 20050527
Entered Medline: 20050526
CONTROLLED TERM: Check Tags: Male
***Antineoplastic Agents, Phytogenic: AE, adverse effects**
Child, Preschool
Cranial Nerve Diseases: CI, chemically induced
Cranial Nerve Diseases: DT, drug therapy
Humans
*Polyneuropathies: CI, chemically induced
*Polyneuropathies: DT, drug therapy
***Pyridoxine: TU, therapeutic use**
***Vincristine: AE, adverse effects**
CAS REGISTRY NO.: 57-22-7 (Vincristine); **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (**Antineoplastic** Agents, Phytogenic)

L219 ANSWER 15 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2005046192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15674885
TITLE: Interventions for photodamaged skin.
AUTHOR: Samuel M; Brooke R C C; Hollis S; Griffiths C E M
CORPORATE SOURCE: Clinical Trials & Epidemiology Research Unit, Ministry Of Health, 226 Outram road, Block A #02-02, Singapore, South East Asia, Singapore.. miny@cteru.com.sg
SOURCE: Cochrane database of systematic reviews (Online : Update Software), (2005) (1) CD001782. Electronic Publication: 2005-01-25. Ref: 75
Journal code: 100909747. ISSN: 1469-493X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(META-ANALYSIS)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050128
Last Updated on STN: 20050528
Entered Medline: 20050527
ABSTRACT:
BACKGROUND: Photodamage describes skin changes such as fine and coarse

wrinkles, roughness, freckles and pigmentation changes that occur as a result of prolonged exposure to the sun. Many treatments are available to reverse the damage, but it is unclear which work and at what cost in terms of unwanted side effects. OBJECTIVES: To assess the effects of topically applied treatments, tablet treatments, laser and surgical procedures for photodamaged skin. SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, Issue 1 2002, MEDLINE (1966-June 2002), EMBASE (1974-June 2002), Health Periodicals (1976-June 2002). We checked references of articles and communicated with authors and the pharmaceutical industry. SELECTION CRITERIA: Randomised controlled trials which compared drug or surgical interventions with no treatment, placebo or another drug, in adults with mild, moderate or severe photodamage of the face or forearms. DATA COLLECTION AND ANALYSIS: Two reviewers independently extracted data and assessed trial quality. MAIN RESULTS: Thirty studies of variable quality were included.Eight trials showed that topical tretinoin cream, in concentrations of 0.02% or higher, was superior to placebo for participants with mild to severe photodamage on the face and forearms (although losses to follow-up were relatively high in most studies). For example, the relative risk of improvement for 0.05% tretinoin cream, compared to placebo (three studies), at 24 weeks, was 1.73 (95% confidence interval 1.39 to 2.14). This effect was not seen for 0.001% topical tretinoin (one study) or 0.01% (three studies). A dose-response relationship was evident for both effectiveness and skin irritation.One small within-patient study showed benefit from topical ascorbic acid compared with placebo.Tazarotene (0.01% to 0.1%) and isotretinoin (0.1%) both showed significant improvement over placebo for moderate photodamage (one study each).There is limited evidence (one trial), to show that the effectiveness of 0.05% tretinoin, is equivalent to the effects of 0.05% and 0.1% tazarotene.One small study showed greater improvement in upper lip wrinkles with CO2 laser technique compared to Baker's phenol chemical peel, at 6 months.Three small RCTs comparing CO2 laser with dermabrasion found no difference in wrinkle score at 4 to 6 months, suggesting that both methods are equally efficacious, but more erythema was reported with the laser.The effectiveness of other interventions such as hydroxy acids and natural polysaccharides was not clear. AUTHORS' CONCLUSIONS: There is conclusive evidence that topical tretinoin improves the appearance of mild to moderate photodamage on the face and forearms, in the short term. However erythema, scaling/dryness, burning/stinging and irritation may be experienced initially.There is limited evidence that tazarotene and isotretinoin benefit patients with moderate photodamage on the face: both are associated with skin irritation and erythema. The effectiveness of other interventions remains uncertain.

CONTROLLED TERM: Administration, Cutaneous
Dermatologic Agents: AE, adverse effects
Dermatologic Agents: TU, therapeutic use
Humans
Isotretinoin: TU, therapeutic use
Keratosis: DT, drug therapy
Laser Surgery: AE, adverse effects
Laser Surgery: MT, methods
Nicotinic Acids: TU, therapeutic use
Randomized Controlled Trials
*Skin Aging
Skin Aging: DE, drug effects
*Skin Diseases: TH, therapy
*Sunlight: AE, adverse effects
Tretinoin: AE, adverse effects
Tretinoin: TU, therapeutic use

CAS REGISTRY NO.: 118292-40-3 (tazarotene); 302-79-4 (Tretinoin); 4759-48-2 (Isotretinoin)

CHEMICAL NAME: 0 (Dermatologic Agents); 0 (Nicotinic Acids)

L219 ANSWER 16 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2003289761 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12817117
TITLE: Clinical trials. Diabetes' brave new world.
AUTHOR: Couzin Jennifer
SOURCE: Science, (2003 Jun 20) 300 (5627) 1862-5.
Journal code: 0404511. ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030621
Last Updated on STN: 20030713
Entered Medline: 20030711
CONTROLLED TERM: Adolescent
Adult
Autoantibodies: IM, immunology
Child
*Clinical Trials
*Diabetes Mellitus, Type 1: DT, drug therapy
Diabetes Mellitus, Type 1: GE, genetics
Diabetes Mellitus, Type 1: IM, immunology
*Diabetes Mellitus, Type 1: PC, prevention & control
Disease Progression
Humans
Immunosuppressive Agents: AE, adverse effects
Immunosuppressive Agents: TU, therapeutic use
Infant
Infant Food
Insulin: AD, administration & dosage
Insulin: TU, therapeutic use
Islets of Langerhans: IM, immunology
Muromonab-CD3: AE, adverse effects
Muromonab-CD3: TU, therapeutic use
National Institutes of Health (U.S.)
Niacinamide: AD, administration & dosage
Niacinamide: TU, therapeutic use
Peptides: TU, therapeutic use
Risk Factors
T-Lymphocytes: IM, immunology
Twin Studies
United States
CAS REGISTRY NO.: 11061-68-0 (Insulin); 98-92-0 (Niacinamide)
CHEMICAL NAME: 0 (Autoantibodies); 0 (Immunosuppressive Agents); 0 (Muromonab-CD3); 0 (Peptides); 0 (monoclonal antibody huOKT3(Ala-Ala))

L219 ANSWER 17 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2003051602 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12503944
TITLE: Niacin-ER and lovastatin treatment of hypercholesterolemia and mixed dyslipidemia.
AUTHOR: Yim Barbara T; Chong Pang H
CORPORATE SOURCE: Department of Pharmacy Practice, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, USA.
SOURCE: Annals of pharmacotherapy, (2003 Jan) 37 (1) 106-15. Ref: 56
Journal code: 9203131. ISSN: 1060-0280.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030204
Last Updated on STN: 20030425
Entered Medline: 20030424

ABSTRACT:
OBJECTIVE: To review the currently available information on the once-daily combination of niacin extended-release (ER)/lovastatin in the treatment of patients with hypercholesterolemia and mixed dyslipidemia at high risk for cardiovascular events. DATA SOURCES: MEDLINE (1966-July 2002) was searched for primary and review articles. Data from the manufacturer were also included. STUDY SELECTION/DATA EXTRACTION: All articles and product labeling deemed relevant to the combination of niacin and statins (i.e., lovastatin) were included for review. English-language studies selected for inclusion were limited to those with human subjects. DATA SYNTHESIS: The Food and Drug Administration approved a new fixed-dose combination of niacin-ER/lovastatin, which is administered once daily. The efficacy and safety of the combined agent have been proven to be similar to either component used alone or in combination for management of hyperlipidemia and mixed dyslipidemia. CONCLUSIONS: Elevated low-density lipoprotein cholesterol (LDL-C) is independently associated with a higher risk for cardiovascular events. Lowering of elevated LDL-C concentrations with statin monotherapy may be insufficient in patients at high risk for cardiovascular events. In fact, consideration of elevated triglycerides (TGs) and/or low concentrations of high-density lipoprotein cholesterol (HDL-C) in patients with elevated LDL-C places them at greater risk. The addition of niacin may enhance or improve the lipid profile of those who require a further decrease of TGs and/or increase of HDL-C even after stable statin therapy. Niacin-ER offers efficacy similar to that of immediate-release niacin, but minimal myopathy and ***hepatotoxicity*** (compared with sustained-release niacin). Although no clinical outcomes are available, current evidence shows that the combination product offers adequate lowering of LDL-C and TGs and increasing HDL-C. The data suggest that therapy with the niacin-ER and lovastatin combination product is safe and does not increase the incidence of adverse effects.

CONTROLLED TERM: Antilipemic Agents: AE, adverse effects
Antilipemic Agents: PD, pharmacology
*Antilipemic Agents: TU, therapeutic use
Clinical Trials
Delayed-Action Preparations
Drug Combinations
Humans
Hyperlipidemia: DT, drug therapy
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AE, adverse effects
Lovastatin: PD, pharmacology
*Lovastatin: TU, therapeutic use
Niacin: AE, adverse effects
Niacin: PD, pharmacology
***Niacin: TU, therapeutic use**

CAS REGISTRY NO.: 59-67-6 (Niacin); 75330-75-5 (Lovastatin)
CHEMICAL NAME: 0 (Antilipemic Agents); 0 (Delayed-Action Preparations); 0 (Drug Combinations); 0 (Lipoproteins, HDL Cholesterol); 0 (Lipoproteins, LDL Cholesterol)

L219 ANSWER 18 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2002142534 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11873395
TITLE: The optimum dose of nicotinamide for protection of pancreatic beta-cells against the **cytotoxic** effect of streptozotocin in albino rat.
AUTHOR: Hassan N; Janjua M Z
CORPORATE SOURCE: Department of Anatomy, Dow Medical College, Karachi.
SOURCE: Journal of Ayub Medical College, Abbottabad : JAMC, (2001 Jul-Sep) 13 (3) 26-30.
Journal code: 8910750. ISSN: 1025-9589.
PUB. COUNTRY: Pakistan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020326
Entered Medline: 20020325

ABSTRACT:
BACKGROUND: The natural course of Insulin Dependent Diabetes Mellitus is characterized by progressive destruction of insulin producing beta-cells of the pancreas resulting from an autoimmune process. The **toxic** effect of some beta-cells toxins like streptozotocin (used to produce animal models of IDDM) has been associated with the oxidative stress due to enhanced DNA repair and NAD depletion in damaged beta-cells. This activity of streptozotocin has been prevented with the use of nicotinamide. METHODS: A light microscopic study was designed to determine the optimum dose of nicotinamide required for protection of pancreatic beta-cells against the **toxicity** of streptozotocin. 35 adult male albino rats were divided into five equal groups A, B, C, D and E. the duration of study was 14 days. The animals in experimental groups C, D and E received a single intraperitoneal injection of nicotinamide 250 mg/Kg, 350 mg/Kg and 500 mg/Kg respectively on day one. Animals in group A and B acted as normal control and diabetic control respectively. All the animals except those in group A received simultaneous injection of streptozotocin 32 mg/Kg body weight intraperitoneally in a single dose. Fasting blood glucose was assessed and the animals weighed before starting the treatment, after 48 hours and at the end of the experimental period. Histological studies were carried out at the end of the study period. RESULTS: The blood glucose level and the final body weight of the animals in group C matched the values in diabetic control. Histologically the pancreas had generally reduced beta-cells mass ($P < 0.001$) with altered morphology. The animals in group D showed impaired glucose tolerance at 48 hours but were normoglycaemic at the end of the study period. There was some loss of beta-cells but a significant number of these cells ($P < 0.05$) showing normal morphology were saved. The animals in group E had normal number of beta-cells having normal morphological features. The final body weight and fasting blood glucose of these animals matched the values in normal control (group A). CONCLUSIONS: These data suggest that the optimum dose of nicotinamide in regard to prevention against the beta-**cytotoxic** effect of streptozotocin in albino rat is 500 mg/Kg body weight.

CONTROLLED TERM: Check Tags: Male
Animals
Anti-Bacterial Agents: AE, adverse effects
*Anti-Bacterial Agents: AI, antagonists & inhibitors
Diabetes Mellitus, Experimental: CI, chemically induced
Diabetes Mellitus, Experimental: PA, pathology
*Diabetes Mellitus, Experimental: PC, prevention & control
Disease Models, Animal
*Islets of Langerhans: DE, drug effects

Islets of Langerhans: PA, pathology
***Niacinamide: AD, administration & dosage**
Niacinamide: TU, therapeutic use
Oxidative Stress
Rats
Streptozocin: AE, adverse effects
*Streptozocin: AI, antagonists & inhibitors
CAS REGISTRY NO.: 18883-66-4 (Streptozocin); 98-92-0 (Niacinamide)
CHEMICAL NAME: 0 (Anti-Bacterial Agents)

L219 ANSWER 19 OF 50 MEDLINE on STN
ACCESSION NUMBER: 1999233197 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10218829
TITLE: A new antioxidative vitamin B6 analogue modulates pathophysiological cell proliferation and damage.
AUTHOR: Kesel A J; Sonnenbichler I; Polborn K; Gurtler L; Klinkert W E; Modolell M; Nussler A K; Oberthur W
CORPORATE SOURCE: Max-Planck-Institut fur Biochemie, Martinsried, Germany.
SOURCE: Bioorganic & medicinal chemistry, (1999 Feb) 7 (2) 359-67. Journal code: 9413298. ISSN: 0968-0896.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990719

ABSTRACT:
The new large scale synthesis of the yellow colored vitamin B6 analogue 5'-O-phosphono-pyridoxylidenerhodanine (2) (B6PR) leads to oligohydrates of its monosodium salt (4). The light-red hemiheptadecahydrate (8 1/2 hydrate) (4a) was crystallized and its three-dimensional structure determined by X-ray crystallography. Special nucleotide and protein interaction properties together with scavenging antioxidative function are combined in this simple water-soluble vitamin B6 analogues B6PR. High (mM) concentrations were untoxic to 'healthy' not affected cells and primary tissues. Complexation of ions (e.g. Ca2+, Fe2+, and Zn2+), modulation of nitric oxide synthases (NOS I-III), nitric oxide (NO) metabolism, and reactive oxygen species (ROS) was found. Special **cytoprotecting**, immunomodulating, stimulating and inhibiting activities were observed in vitro, not in comparison with some natural and synthetic pyridoxines. Low B6PR suppressed proliferation, high induced selective cell death of some cancer cell lines. Low B6PR protected HIV-1-infected CD4+ HUT 78 cells against HIV-1-mediated destruction (complete inhibition of HIV-1-induced syncytia formation and cell death) and reduced p24 level. Autoreactive S100beta-specific T cells of Lewis rat, a model of multiple sclerosis, could be influenced. Oxidative damage and age, acquired and inherited disease related pathophysiological disorders can be treated by this new cytopathology-selective versatile acting B6PR.

CONTROLLED TERM: Animals
Bone Marrow Cells: DE, drug effects
CD4-Positive T-Lymphocytes: DE, drug effects
*Cell Division: DE, drug effects
Crystallography, X-Ray
Dose-Response Relationship, Drug
HIV-1: ME, metabolism
Humans
Mice
Models, Biological
Models, Chemical

Models, Molecular
Nitrites: ME, metabolism
*Pyridoxine: AA, analogs & derivatives
*Pyridoxine: CH, chemistry
Rats
Research Support, Non-U.S. Gov't
Time Factors
Tumor Cells, Cultured
CAS REGISTRY NO.: **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (Nitrites)

L219 ANSWER 20 OF 50 MEDLINE on STN
ACCESSION NUMBER: 1999388955 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10461859
TITLE: Nicotinamide and methionine reduce the liver **toxic** effect of methotrexate.
AUTHOR: Kroger H; Hauschild A; Ohde M; Bache K; Voigt W P; Thefeldt W; Kruger D
CORPORATE SOURCE: Deutsches Rheumaforschungszentrum Berlin, Germany.
SOURCE: General pharmacology, (1999 Aug) 33 (2) 203-6.
Journal code: 7602417. ISSN: 0306-3623.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991022

ABSTRACT:
Methotrexate is widely used as a therapeutic agent in different diseases. This therapy is connected with various side effects, including liver ***toxicity.*** We have developed a mouse model to demonstrate the ***toxic*** effects of methotrexate: mice were given 50 mg/kg acetaminophen, which itself has no effect on the liver. If, additionally, methotrexate is applied, there is an increase in the death rate, as well as in glutamate-oxaloacetate transaminase (GOT) and glutamate-pyruvate transaminase (GPT) activities. If methotrexate is administered in conjunction with either nicotinamide or methionine, the rise in the death rate and in GOT and GPT activities associated with methotrexate application is markedly reduced. On the basis of these results, it can be concluded that methotrexate therapy should be combined with either nicotinamide or methionine, respectively.

CONTROLLED TERM: Check Tags: Male
Acetaminophen: TU, therapeutic use
Alanine Transaminase: BL, blood
Alanine Transaminase: DE, drug effects
Analgesics, Non-Narcotic: TU, therapeutic use
Animals
*Antirheumatic Agents: AE, adverse effects
Aspartate Aminotransferases: BL, blood
Aspartate Aminotransferases: DE, drug effects
Drug Therapy, Combination
*Liver Diseases: CI, chemically induced
Liver Diseases: DT, drug therapy
*Methionine: TU, therapeutic use
***Methotrexate: AE, adverse effects**
Mice
Mice, Inbred DBA
***Niacinamide: TU, therapeutic use**
CAS REGISTRY NO.: 103-90-2 (Acetaminophen); 59-05-2 (Methotrexate); 63-68-3

(Methionine); 98-92-0 (Niacinamide)
CHEMICAL NAME: 0 (Analgesics, Non-Narcotic); 0 (Antirheumatic Agents); EC 2.6.1.1 (Aspartate Aminotransferases); EC 2.6.1.2 (Alanine Transaminase)

L219 ANSWER 21 OF 50 MEDLINE on STN
ACCESSION NUMBER: 1998289781 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9626479
TITLE: Efficacy of pyridoxine to ameliorate the cutaneous toxicity associated with doxorubicin containing pegylated (Stealth) liposomes: a randomized, double-blind clinical trial using a canine model.
AUTHOR: Vail D M; Chun R; Thamm D H; Garrett L D; Cooley A J; Obradovich J E
CORPORATE SOURCE: Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin, Madison 53706, USA.. vaild@svm.vetmed.wisc.edu
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (1998 Jun) 4 (6) 1567-71.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980827

ABSTRACT:
A cutaneous reaction termed palmar-plantar erythrodysesthesia (PPES) or hand-foot syndrome can be dose limiting for Doxil, a doxorubicin containing pegylated (Stealth) liposome. The objective of this study was to determine the ability of concomitant pyridoxine therapy to prevent the development of PPES during Doxil therapy. Forty-one dogs with non-Hodgkin's lymphoma were randomized in a double-blind fashion to receive either oral pyridoxine or placebo daily during Doxil chemotherapy (1.0 mg/kg, i.v., every 3 weeks for a total of five treatments). Cutaneous toxicity was determined by clinical and histological scoring. No difference was observed in remission rates (71.4 versus 75%) achieved between groups. The likelihood of developing serious PPES and having to decrease or discontinue Doxil therapy was 4.2 times (relative risk) greater in placebo group dogs than in pyridoxine group dogs (P = 0.032). Pyridoxine did not completely abrogate PPES; however, it occurred later and less dramatically than in placebo-treated dogs and resulted in fewer treatment delays or discontinuations, allowing a higher cumulative dose of Doxil to be received. Compared to the 5.0 mg/kg cumulative target dose, pyridoxine-treated dogs received a median cumulative dose of 4.7 mg/kg (mean, 4.1 mg/kg), and the placebo-treated dogs received a median of 2.75 mg/kg (mean, 2.9 mg/kg; P < 0.028). A trend (P = 0.084) toward prolongation of remission length was observed in dogs receiving pyridoxine, which was likely attributable to their ability to receive more Doxil without delay or discontinuation. We conclude that pyridoxine is effective in delaying the onset and severity of PPES in this canine model.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Male
Animals
***Antibiotics, Antineoplastic: AE, adverse effects**
Antibiotics, Antineoplastic: TU, therapeutic use
*Dog Diseases: DT, drug therapy

Dog Diseases: MO, mortality
Dog Diseases: PA, pathology
Dogs
Double-Blind Method
Doxorubicin: AD, administration & dosage
***Doxorubicin: AE, adverse effects**
Doxorubicin: TU, therapeutic use
Drug Carriers
Liposomes
Lymphoma, Non-Hodgkin: DT, drug therapy
Lymphoma, Non-Hodgkin: MO, mortality
Lymphoma, Non-Hodgkin: PA, pathology
*Lymphoma, Non-Hodgkin: VE, veterinary
Neoplasm Staging
***Pyridoxine: TU, therapeutic use**
Skin: DE, drug effects
*Skin: PA, pathology
Survival Analysis
Time Factors

CAS REGISTRY NO.: 23214-92-8 (Doxorubicin); **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (Antibiotics, **Antineoplastic**); 0 (Drug Carriers); 0 (Liposomes)

L219 ANSWER 22 OF 50 MEDLINE on STN
ACCESSION NUMBER: 1998215103 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9555819
TITLE: Topical treatment of acne vulgaris: retinoids and cutaneous irritation.
AUTHOR: Leyden J J
CORPORATE SOURCE: Department of Dermatology, University of Pennsylvania School of Medicine, Philadelphia, USA.
SOURCE: Journal of the American Academy of Dermatology, (1998 Apr) 38 (4) S1-4. Ref: 17
Journal code: 7907132. ISSN: 0190-9622.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980505
CONTROLLED TERM: *Acne Vulgaris: DT, drug therapy
Administration, Topical
Anti-Inflammatory Agents, Non-Steroidal: AD, administration & dosage
Gels
Humans
*Keratolytic Agents: AD, administration & dosage
Keratolytic Agents: AE, adverse effects
Naphthalenes: AD, administration & dosage
Nicotinic Acids: AD, administration & dosage
Ointments
Research Support, Non-U.S. Gov't
*Retinoids: AD, administration & dosage
Retinoids: AE, adverse effects
Tretinoin: AD, administration & dosage
Tretinoin: AE, adverse effects

CAS REGISTRY NO.: 106685-40-9 (adapalene); 118292-40-3 (tazarotene); 302-79-4 (Tretinoin)
CHEMICAL NAME: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Gels); 0 (Keratolytic Agents); 0 (Naphthalenes); 0 (Nicotinic Acids); 0 (Ointments); 0 (Retinoids)

L219 ANSWER 23 OF 50 MEDLINE on STN
ACCESSION NUMBER: 97471114 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9330055
TITLE: Pellagra, azathioprine and inflammatory bowel disease.
AUTHOR: Jarrett P; Duffill M; Oakley A; Smith A
CORPORATE SOURCE: Department of Dermatology, Health Waikato, Hamilton, New Zealand.
SOURCE: Clinical and experimental dermatology, (1997 Jan) 22 (1) 44-5.
Journal code: 7606847. ISSN: 0307-6938.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971024
CONTROLLED TERM: Check Tags: Female
Adolescent
Adult
***Azathioprine: AE, adverse effects**
*Colitis, Ulcerative: DT, drug therapy
Humans
***Immunosuppressive Agents: AE, adverse effects**
Niacinamide: TU, therapeutic use
*Pellagra: CI, chemically induced
Pellagra: DT, drug therapy
CAS REGISTRY NO.: 446-86-6 (Azathioprine); 98-92-0 (Niacinamide)
CHEMICAL NAME: 0 (Immunosuppressive Agents)

L219 ANSWER 24 OF 50 MEDLINE on STN
ACCESSION NUMBER: 93353547 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8102408
TITLE: Pyridoxine therapy for palmar-plantar erythrodysesthesia associated with taxotere.
AUTHOR: Vukelja S J; Baker W J; Burris H A 3rd; Keeling J H; Von Hoff D
SOURCE: Journal of the National Cancer Institute, (1993 Sep 1) 85 (17) 1432-3.
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19931001
Last Updated on STN: 19960129
Entered Medline: 19930914
CONTROLLED TERM: Check Tags: Female; Male
***Antineoplastic Agents, Phytogenic: AE, adverse effects**

Erythema: DT, drug therapy
Foot Dermatoses: CI, chemically induced
*Foot Dermatoses: DT, drug therapy
Hand Dermatoses: CI, chemically induced
*Hand Dermatoses: DT, drug therapy
Humans
Middle Aged
Paclitaxel: AE, adverse effects
*Paclitaxel: AA, analogs & derivatives
Paresthesia: DT, drug therapy
***Pyridoxine: TU, therapeutic use**
*Taxoids

CAS REGISTRY NO.: 114977-28-5 (docetaxel); 33069-62-4 (Paclitaxel); **65-23-6 (Pyridoxine)**

CHEMICAL NAME: 0 (**Antineoplastic** Agents, Phytogenic); 0 (Taxoids)

L219 ANSWER 25 OF 50 MEDLINE on STN
ACCESSION NUMBER: 93277806 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8504053
TITLE: Pellagra secondary to 5-fluorouracil.
AUTHOR: Stevens H P; Ostlere L S; Begent R H; Dooley J S; Rustin M H
CORPORATE SOURCE: Department of Dermatology, Royal Free Hospital and School of Medicine, London, U.K.
SOURCE: British journal of dermatology, (1993 May) 128 (5) 578-80. Journal code: 0004041. ISSN: 0007-0963.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199307
ENTRY DATE: Entered STN: 19930716
Last Updated on STN: 19930716
Entered Medline: 19930707

ABSTRACT:
The development of pellagra in a patient treated with 5-fluorouracil for malignant disease is reported. The aetiology of pellagra in this patient is discussed, and the reasons for possible under-diagnosis of pellagra in association with malignant disease considered. We report a patient who presented with the typical skin changes of pellagra. The rash, and an associated acute deterioration in cerebral function, were exacerbated by treatment with 5-fluorouracil. The importance of considering nicotinic-acid deficiency in patients with malignant disease has not been emphasized in the literature.

CONTROLLED TERM: Check Tags: Male
Aged
Biliary Tract Neoplasms: DT, drug therapy
***Fluorouracil: AE, adverse effects**
Fluorouracil: TU, therapeutic use
Humans
Liver Neoplasms: DT, drug therapy
Liver Neoplasms: SC, secondary
Nicotinic Acids: TU, therapeutic use
*Pellagra: CI, chemically induced
Pellagra: DT, drug therapy
Pellagra: PA, pathology
Skin: PA, pathology

CAS REGISTRY NO.: 51-21-8 (Fluorouracil)

CHEMICAL NAME: 0 (Nicotinic Acids)

L219 ANSWER 26 OF 50 MEDLINE on STN
ACCESSION NUMBER: 92377616 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1380762
TITLE: Taurine and niacin offer a novel therapeutic modality in prevention of chemically-induced pulmonary fibrosis in hamsters.
AUTHOR: Giri S N; Wang Q
CORPORATE SOURCE: Department of Veterinary Pharmacology and Toxicology, University of California, Davis 95616.
CONTRACT NUMBER: 2R01 HL27354 (NHLBI)
SOURCE: Advances in experimental medicine and biology, (1992) 315 329-40.
Journal code: 0121103. ISSN: 0065-2598.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19921009
Last Updated on STN: 19960129
Entered Medline: 19920918

ABSTRACT:
The bleomycin (BL)-hamster model of interstitial pulmonary fibrosis (IPF) is generally associated with increased lung lipid peroxidation, measured as malondialdehyde equivalent (MDAE), calcium and collagen content; and superoxide dismutase (SOD), prolyl hydroxylase (PH) and poly(ADP-ribose) polymerase activities. We found that combined treatment with taurine in drinking water (1%) and niacin IP (250 mg/kg) daily, significantly decreased the BL-induced increases in lung MDAE and calcium content, and SOD, PH and poly(ADP-ribose) polymerase activities. This treatment almost completely ameliorated the BL-induced increases in the lung collagen accumulation as well. Findings of a similar nature were also demonstrated when taurine (2.5%) and niacin (2.5%) were supplemented in the diet of hamsters used in the same BL model of IPF. The diet supplemented with taurine (2.5%), niacin (2.5%), or taurine (2.5%) + niacin (2.5%) also reduced AD-induced increases in lung collagen accumulation, phospholipids, MDAE and SOD activity. It was concluded that diet supplemented with taurine and/or niacin would completely or partially ameliorate chemically-induced pulmonary fibrosis.

CONTROLLED TERM: *Amiodarone: AE, adverse effects
Animals
***Bleomycin: AE, adverse effects**
Drug Therapy, Combination
Hamsters
***Niacin: TU, therapeutic use**
*Pulmonary Fibrosis: CI, chemically induced
*Pulmonary Fibrosis: PC, prevention & control
Research Support, U.S. Gov't, P.H.S.
*Taurine: TU, therapeutic use
CAS REGISTRY NO.: 107-35-7 (Taurine); 11056-06-7 (Bleomycin); 1951-25-3 (Amiodarone); 59-67-6 (Niacin)

L219 ANSWER 27 OF 50 MEDLINE on STN
ACCESSION NUMBER: 92136135 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1735009
TITLE: Hexamethylmelamine and low or moderate dose cisplatin with or without pyridoxine for treatment of advanced ovarian carcinoma: a study of the Eastern Cooperative Oncology Group.

AUTHOR: Wiernik P H; Yeap B; Vogl S E; Kaplan B H; Comis R L; Falkson G; Davis T E; Fazzini E; Cheuvart B; Horton J
CORPORATE SOURCE: Albert Einstein Cancer Center, Bronx, New York.
CONTRACT NUMBER: CA 14958 (NCI)
CA 18281 (NCI)
CA 23318 (NCI)
SOURCE: Cancer investigation, (1992) 10 (1) 1-9.
Journal code: 8307154. ISSN: 0735-7907.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920329
Last Updated on STN: 19920329
Entered Medline: 19920312

ABSTRACT:
A total of 248 analyzable patients with Stages III-IV ovarian epithelial cancer (114 with and 134 without prior chemotherapy) were randomized to one of four cisplatin (DDP)-hexamethylmelamine (HMM) regimens. In each, HMM, 200 mg/m2 was given orally daily on days 8-21 of each 21-day cycle. DDP was given i.v. on Day 1 at a dose of 37.5 mg/m2 (regimens A and B) or 75 mg/m2 (regimens C and D). In addition, since pyridoxine administration has been reported to reduce the neurotoxicity of HMM, that agent was given at a dose of 300 mg/m2 orally on Days 1-21 in regimens B and D. Randomization was stratified for performance status (0-1, 2-3) and largest tumor diameter at entry (greater than 2- less than or equal to 10 cm, greater than 10 cm) for previously untreated patients, and for performance status and time from initial diagnosis to entry on study (less than or equal to 1 year, greater than 1 year) for previously treated patients. The overall response rate (PR + CR) was 54%, with 25% of patients achieving a complete response. The 61% response rate with the higher dose DDP regimens was significantly greater than the 47% response rate with the lower dose regimens ($p = 0.031$). Multivariate analysis identified higher DDP dose, age less than 60 years, no prior chemotherapy, small tumor bulk and favorable tumor grade as significant prognosticators for response. The overall median response duration was 8.3 months (range 1-70 months). Prior chemotherapy, pyridoxine administration, recent diagnosis, and large tumor size were identified by multivariate analysis as factors adversely affecting response duration. Patients treated with the higher dose DDP regimens had more severe nausea, vomiting, and neurotoxicity. This study demonstrates that the combination of DDP + HMM is an effective regimen for advanced ovarian carcinoma that yields response rates comparable to other more complex regimens, and that there is a dose-response relationship for DDP in ovarian cancer. Although pyridoxine administration significantly reduced neurotoxicity, its adverse effect on response duration suggests that the agent should not be administered with DDP or HMM. The mechanism by which pyridoxine may unfavorably affect response duration deserves further investigation.

CONTROLLED TERM: Check Tags: Female
Altretamine: AD, administration & dosage
Altretamine: AE, adverse effects
***Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use**
Cisplatin: AD, administration & dosage
Cisplatin: AE, adverse effects
Drug Administration Schedule
Humans
Neoplasm Staging

*Ovarian Neoplasms: DT, drug therapy
Ovarian Neoplasms: MO, mortality
Ovarian Neoplasms: PA, pathology
Pyridoxine: AD, administration & dosage
Pyridoxine: AE, adverse effects
Research Support, U.S. Gov't, P.H.S.
Survival Analysis
CAS REGISTRY NO.: 15663-27-1 (Cisplatin); 645-05-6 (Altretamine); **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (**Antineoplastic** Combined Chemotherapy Protocols)

L219 ANSWER 28 OF 50 MEDLINE on STN
ACCESSION NUMBER: 91266533 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1828751
TITLE: Diabetes, cyclosporin **nephrotoxicity**, and serum creatinine concentration.
COMMENT: Comment on: Diabet Med. 1990 Sep-Oct;7(8):731-5. PubMed ID: 2147636
AUTHOR: McNally P G; Feehally J; Walls J
SOURCE: Diabetic medicine : a journal of the British Diabetic Association, (1991 Apr) 8 (3) 289.
Journal code: 8500858. ISSN: 0742-3071.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910811
Last Updated on STN: 19910811
Entered Medline: 19910723
CONTROLLED TERM: *Creatinine: BL, blood
***Cyclosporins: AE, adverse effects**
Cyclosporins: TU, therapeutic use
Diabetes Mellitus, Type 1: BL, blood
*Diabetes Mellitus, Type 1: DT, drug therapy
Glomerular Filtration Rate
Humans
Kidney: DE, drug effects
*Kidney: PA, pathology
Kidney: PP, physiopathology
Kidney Function Tests
Niacinamide: TU, therapeutic use
CAS REGISTRY NO.: 60-27-5 (Creatinine); 98-92-0 (Niacinamide)
CHEMICAL NAME: 0 (Cyclosporins)

L219 ANSWER 29 OF 50 MEDLINE on STN
ACCESSION NUMBER: 88125202 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3340642
TITLE: Lovastatin alone and in combination for treatment of primary hypercholesterolemia.
AUTHOR: Stein E A; Lamkin G E; Bewley D Z
CORPORATE SOURCE: Cholesterol Treatment Center, University of Cincinnati Medical Center, Ohio 45267-0714.
SOURCE: Progress in clinical and biological research, (1988) 255 281-93.
Journal code: 7605701. ISSN: 0361-7742.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880323
CONTROLLED TERM: Check Tags: Female; Male
Adult
Aged
Anion Exchange Resins: TU, therapeutic use
Drug Therapy, Combination
Humans
*Hypercholesterolemia: DT, drug therapy
Hypercholesterolemia, Familial: DT, drug therapy
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AE, adverse effects
*Lovastatin: TU, therapeutic use
Middle Aged
Niacin: TU, therapeutic use
Patient Compliance
Research Support, Non-U.S. Gov't
CAS REGISTRY NO.: 59-67-6 (Niacin); 75330-75-5 (Lovastatin)
CHEMICAL NAME: 0 (Anion Exchange Resins); 0 (Lipoproteins, HDL Cholesterol); 0 (Lipoproteins, LDL Cholesterol)

L219 ANSWER 30 OF 50 MEDLINE on STN
ACCESSION NUMBER: 89217546 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2977417
TITLE: [Prevention of disorders of cardiac contractility with nicotinamide in adriblastin -related damage]. Preduprezhdenie narushenii sokratitel'noi funktsii serdtsa pri adriblastinovom povrezhdenii s pomoshch'iu nikotinamida.
AUTHOR: Nurmukhambetov A N; Riabtseva T A
SOURCE: Kardiologiia, (1988 Dec) 28 (12) 91-3.
Journal code: 0376351. ISSN: 0022-9040.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198905
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890530

ABSTRACT:
Pretreatment with 20 mg/kg nicotinamide 3 days prior to a single intraperitoneal 6 mg/kg adriblastin injection, followed by repeated injections every second days for 1 week, prevented cardiac contractility disorders in adriblastin-treated rats, while their cardiac contractility was less prone to hypoxic depression and recovered better at subsequent reoxygenation.

CONTROLLED TERM: Animals
Anoxia: CI, chemically induced
*Anoxia: DT, drug therapy
Cardiomyopathies: CI, chemically induced
*Cardiomyopathies: DT, drug therapy
***Doxorubicin: AE, adverse effects**
English Abstract
Heart Failure, Congestive: ET, etiology
*Heart Failure, Congestive: PC, prevention & control

*Myocardial Contraction: DE, drug effects
***Niacinamide: TU, therapeutic use**
Rats
CAS REGISTRY NO.: 23214-92-8 (Doxorubicin); 98-92-0 (Niacinamide)

L219 ANSWER 31 OF 50 MEDLINE on STN
ACCESSION NUMBER: 87297218 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2956917
TITLE: [Drug-induced pellagroid erythema. A case of pellagroid erythema caused by isoniazide].
Les erythemes pellagroides medicamenteux. Une observation d'erytheme pellagroide secondaire a l'isoniazide.
AUTHOR: Schmutz J L; Cuny J F; Trechot P; Weber M; Beurey J
SOURCE: Annales de dermatologie et de venereologie, (1987) 114 (4) 569-76.
Journal code: 7702013. ISSN: 0151-9638.
PUB. COUNTRY: France
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198709
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19870903
CONTROLLED TERM: Check Tags: Female
Antineoplastic Agents: AE, adverse effects
*Erythema: CI, chemically induced
Ethionamide: AE, adverse effects
Humans
*Isoniazid: AE, adverse effects
Middle Aged
Monoamine Oxidase Inhibitors: AE, adverse effects
Niacinamide: ME, metabolism
*Pellagra: CI, chemically induced
Pellagra: DT, drug therapy
Pyrazinamide: AE, adverse effects
Pyridoxine: TU, therapeutic use
Skin: ME, metabolism
CAS REGISTRY NO.: 536-33-4 (Ethionamide); 54-85-3 (Isoniazid); **65-23-6 (Pyridoxine)**; 98-92-0 (Niacinamide); 98-96-4 (Pyrazinamide)
CHEMICAL NAME: 0 (**Antineoplastic** Agents); 0 (Monoamine Oxidase Inhibitors)

L219 ANSWER 32 OF 50 MEDLINE on STN
ACCESSION NUMBER: 84173669 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6369722
TITLE: Systemic therapy for superficial bladder cancer.
AUTHOR: Soloway M S
CONTRACT NUMBER: CA 15934 (NCI)
CA 18643 (NCI)
SOURCE: Urology, (1984 Apr) 23 (4 Suppl) 88-93.
Journal code: 0366151. ISSN: 0090-4295.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198405

ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840515
CONTROLLED TERM: Check Tags: Female; Male
Animals
***Antineoplastic Agents: AD, administration & dosage**
Antineoplastic Agents: AE, adverse effects
Bladder Neoplasms: CI, chemically induced
*Bladder Neoplasms: DT, drug therapy
*Carcinoma in Situ: DT, drug therapy
Cisplatin: AD, administration & dosage
Cisplatin: AE, adverse effects
Clinical Trials
Cyclophosphamide: AD, administration & dosage
Cyclophosphamide: AE, adverse effects
FANFT
Fluorouracil: AD, administration & dosage
Fluorouracil: AE, adverse effects
Humans
Methotrexate: AD, administration & dosage
Methotrexate: AE, adverse effects
Mice
*Neoplasm Recurrence, Local: PC, prevention & control
Pyridoxine: AD, administration & dosage
Pyridoxine: AE, adverse effects
Research Support, U.S. Gov't, P.H.S.
Vitamin A: AD, administration & dosage
Vitamin A: AE, adverse effects
CAS REGISTRY NO.: 11103-57-4 (Vitamin A); 15663-27-1 (Cisplatin); 24554-26-5 (FANFT); 50-18-0 (Cyclophosphamide); 51-21-8 (Fluorouracil); 59-05-2 (Methotrexate); **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (**Antineoplastic** Agents)

L219 ANSWER 33 OF 50 MEDLINE on STN
ACCESSION NUMBER: 82086361 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6274098
TITLE: [Nicotinamide as an effective agent against endogenous hypocorticism during prolonged corticosteroid therapy]. Nikotinamid kak effektivnoe sredstvo protiv endogennogo gipokortitsizma pri dlitel'noi kortikosteroidnoi terapii.
AUTHOR: Vinogradov V V; Tarasov Iu A; Vodoevich V P; Borets V M; Gal'tsev V A
SOURCE: Voprosy pitaniia, (1981 Sep-Oct) (5) 20-3.
Journal code: 2984870R. ISSN: 0042-8833.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198202
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19820212
CONTROLLED TERM: *Adrenal Insufficiency: CI, chemically induced
Adult
*Corticotropin: BL, blood
Drug Interactions
English Abstract
Humans
***Niacinamide: AD, administration & dosage**

Prednisolone: AD, administration & dosage
***Prednisolone: AE, adverse effects**
Rheumatic Diseases: BL, blood
*Rheumatic Diseases: DT, drug therapy
Substance Withdrawal Syndrome: PC, prevention & control
Time Factors
CAS REGISTRY NO.: 50-24-8 (Prednisolone); 9002-60-2 (Corticotropin); 98-92-0 (Niacinamide)

L219 ANSWER 34 OF 50 MEDLINE on STN
ACCESSION NUMBER: 79205214 MEDLINE
DOCUMENT NUMBER: PubMed ID: 452535
TITLE: [Prophylaxis of complications caused by cytostatic drugs used in oncological patients].
Profilaktika oslozhnenii, obuslovlennykh primeneniem tsitostaticheskikh preparatov u onkologicheskikh bol'nykh.
AUTHOR: Bratseva V L
SOURCE: Vrachebnoe delo, (1979 Mar) (3) 6-10.
Journal code: 0413607. ISSN: 0049-6804.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197908
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790816
CONTROLLED TERM: Check Tags: Female; Male
Adolescent
Adult
***Antineoplastic Agents: AE, adverse effects**
Antineoplastic Agents: TU, therapeutic use
Breast Neoplasms: DH, diet therapy
Breast Neoplasms: DT, drug therapy
Child
Chlorides: TU, therapeutic use
Diazepam: TU, therapeutic use
English Abstract
Folic Acid: TU, therapeutic use
Gastrointestinal Neoplasms: DH, diet therapy
Gastrointestinal Neoplasms: DT, drug therapy
Humans
Lung Neoplasms: DH, diet therapy
Lung Neoplasms: DT, drug therapy
Middle Aged
Pyridoxine: TU, therapeutic use
CAS REGISTRY NO.: 439-14-5 (Diazepam); 59-30-3 (Folic Acid); **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (**Antineoplastic** Agents); 0 (Chlorides)

L219 ANSWER 35 OF 50 MEDLINE on STN
ACCESSION NUMBER: 81127385 MEDLINE
DOCUMENT NUMBER: PubMed ID: 555047
TITLE: [Behavior of various B-vitamins following radiation and/or cytostatic treatment of gynecologic carcinomas].
Zum Verhalten einiger B-Vitamine nach Strahlen- und/oder Zytostatikabehandlung gynakologischer Karzinome.
AUTHOR: Ladner H A; Holtz F
SOURCE: Strahlentherapie. Sonderbande, (1978) 75 191-5.
Journal code: 0404544. ISSN: 0371-3822.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198104
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19810421
CONTROLLED TERM: Check Tags: Female
***Antineoplastic Agents: AE, adverse effects**
Genital Neoplasms, Female: CO, complications
*Genital Neoplasms, Female: TH, therapy
Humans
Pyridoxine: TU, therapeutic use
*Radiation Injuries
Riboflavin Deficiency: ET, etiology
Thiamine Deficiency: ET, etiology
*Vitamin B 6 Deficiency: ET, etiology
Vitamin B 6 Deficiency: PC, prevention & control
CAS REGISTRY NO.: **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (**Antineoplastic** Agents)

L219 ANSWER 36 OF 50 MEDLINE on STN
ACCESSION NUMBER: 76105189 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1209536
TITLE: [Pain phenomena due to cancer chemotherapy. their modification under the influence of certain vasodilator agents].
Etude des phenomenes douloureux provoques par la chimiotherapie anti-cancereuse. Leurs modifications sous linfluence de certains agents vaso-dilatateurs.
AUTHOR: Cluzan R; Ramona F; Caillaud J M; Levillain R
SOURCE: Therapie, (1975 Jul-Aug) (4) 617-20.
Journal code: 0420544. ISSN: 0040-5957.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197603
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19760305
CONTROLLED TERM: Check Tags: Female; Male
Aged
***Antineoplastic Agents: AE, adverse effects**
Humans
Isoxsuprine: TU, therapeutic use
Middle Aged
Nafronyl: TU, therapeutic use
Nicotinic Acids: TU, therapeutic use
Pain: CI, chemically induced
*Pain: DT, drug therapy
*Vasodilator Agents: TU, therapeutic use
CAS REGISTRY NO.: 31329-57-4 (Nafronyl); 395-28-8 (Isoxsuprine)
CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Nicotinic Acids); 0 (Vasodilator Agents)

L219 ANSWER 37 OF 50 MEDLINE on STN
ACCESSION NUMBER: 75062509 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4803900

TITLE: Intra-arterial cancer chemotherapy with combined anticancer agents.
AUTHOR: Fujimoto S; Miyoshi T; Nomura Y; Akao T; Ito B
SOURCE: Japanese journal of surgery, (1973 Mar) 3 (1) 32-9.
Journal code: 1302176. ISSN: 0047-1909.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197503
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750310
CONTROLLED TERM: Adult
***Antineoplastic Agents: AD, administration & dosage**
Antineoplastic Agents: AE, adverse effects
Cyclophosphamide: AD, administration & dosage
Cytarabine: AD, administration & dosage
Deoxycytidine: AD, administration & dosage
Drug Therapy, Combination
Fluorouracil: AD, administration & dosage
Humans
Injections, Intra-Arterial
Leukopenia: CI, chemically induced
*Liver Neoplasms: DT, drug therapy
Methotrexate: AD, administration & dosage
Middle Aged
Mitomycins: AD, administration & dosage
*Neoplasms, Connective Tissue: DT, drug therapy
Pyridoxal Phosphate: AD, administration & dosage
*Stomach Neoplasms: DT, drug therapy
Stomach Neoplasms: PA, pathology
Vinblastine: AD, administration & dosage
Vincristine: AD, administration & dosage
CAS REGISTRY NO.: 147-94-4 (Cytarabine); 50-18-0 (Cyclophosphamide); 51-21-8 (Fluorouracil); **54-47-7 (Pyridoxal Phosphate)**; 57-22-7 (Vincristine); 59-05-2 (Methotrexate); 865-21-4 (Vinblastine); 951-77-9 (Deoxycytidine)
CHEMICAL NAME: 0 (**Antineoplastic** Agents); 0 (Mitomycins)

L219 ANSWER 38 OF 50 MEDLINE on STN
ACCESSION NUMBER: 72027726 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4329781
TITLE: Notes on streptozotocin in metastatic insulinoma.
AUTHOR: Vogel T T
SOURCE: Journal of surgical oncology, (1971) 3 (5) 481-5.
Journal code: 0222643. ISSN: 0022-4790.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197201
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19720105
CONTROLLED TERM: Check Tags: Male
*Adenoma, Islet Cell: DT, drug therapy
Adult
Antibiotics, Antineoplastic: AE, adverse effects

*Antibiotics, Antineoplastic: TU, therapeutic use
Autopsy
Blood Glucose
Bone Marrow: DE, drug effects
Bone Marrow: PA, pathology
Brain: PA, pathology
Glucosamine: AE, adverse effects
Glucosamine: TU, therapeutic use
Humans
Immunoassay
Injections, Intra-Arterial
Injections, Intravenous
Insulin: AN, analysis
Kidney: PA, pathology
Liver: PA, pathology
***Liver Neoplasms: DT, drug therapy**
Neoplasm Metastasis
Niacinamide: TU, therapeutic use
*Nitroso Compounds: TU, therapeutic use
Nitrosourea Compounds: AE, adverse effects
Nitrosourea Compounds: TU, therapeutic use
Pancreas: PA, pathology
***Pancreatic Neoplasms: DT, drug therapy**
Thyroid Gland: PA, pathology
Thyroid Neoplasms: DT, drug therapy
*Urea: TU, therapeutic use

CAS REGISTRY NO.: 11061-68-0 (Insulin); 3416-24-8 (Glucosamine); 57-13-6 (Urea); 98-92-0 (Niacinamide)
CHEMICAL NAME: 0 (Antibiotics, Antineoplastic); 0 (Blood Glucose); 0 (Nitroso Compounds); 0 (Nitrosourea Compounds)

L219 ANSWER 39 OF 50 MEDLINE on STN
ACCESSION NUMBER: 72060257 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4108245
TITLE: [Experiences with ambulatory intermittent cytostatic treatment of bronchial cancer].
Experiences avec le traitement cytostatique amublatoire intermittent du cancer bronchique.
AUTHOR: Macholda F; Bohut V; Votava V; Pavlova P; Mericka O; Sajnerova B
SOURCE: Les Bronches, (1971 Mar-Apr) 21 (2) 197-201.
Journal code: 7700862. ISSN: 0007-2222.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197202
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19720216
CONTROLLED TERM: Ambulatory Care
***Antineoplastic Agents: TU, therapeutic use**
*Bronchial Neoplasms: DT, drug therapy
Bronchial Neoplasms: MO, mortality
*Cyclophosphamide: AD, administration & dosage
Cyclophosphamide: AE, adverse effects
Humans
Leukopenia: CI, chemically induced
*Lung Neoplasms: DT, drug therapy
Lung Neoplasms: MO, mortality

Palliative Care
Prognosis
***Pyridoxine: TU, therapeutic use**
*Triaziquone: TU, therapeutic use
CAS REGISTRY NO.: 50-18-0 (Cyclophosphamide); **65-23-6 (Pyridoxine)**; 68-76-8 (Triaziquone)
CHEMICAL NAME: 0 (**Antineoplastic** Agents)

L219 ANSWER 40 OF 50 MEDLINE on STN
ACCESSION NUMBER: 70051976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4901557
TITLE: [Complex treatment of late radiation injuries of the skin by use of prodigiozan].
Kompleksnoe lechenie pozhnikh luchevykh povrezhdenii kozhi s primeneniem prodigiozana.
AUTHOR: Bardychev M S; Vaisberg G E; Givsktalv N I
SOURCE: Antibiotiki, (1969 Oct) 14 (10) 943-7.
Journal code: 0375020. ISSN: 0003-5637.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197001
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19700120
CONTROLLED TERM: Check Tags: Female; Male
Adult
Aged
Antineoplastic Agents: AE, adverse effects
***Antineoplastic Agents: TU, therapeutic use**
Ascorbic Acid: TU, therapeutic use
Diphenhydramine: TU, therapeutic use
Humans
Middle Aged
Polysaccharides, Bacterial: AE, adverse effects
*Polysaccharides, Bacterial: TU, therapeutic use
Pyridoxine: TU, therapeutic use
*Radiodermatitis
Regeneration: DE, drug effects
Serratia marcescens
Skin: DE, drug effects
Stimulation, Chemical
Thiamine: TU, therapeutic use
CAS REGISTRY NO.: 50-81-7 (Ascorbic Acid); 58-73-1 (Diphenhydramine); 59-43-8 (Thiamine); **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (**Antineoplastic** Agents); 0 (Polysaccharides, Bacterial)

L219 ANSWER 41 OF 50 MEDLINE on STN
ACCESSION NUMBER: 68132718 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6081720
TITLE: [Treatment of the secondary collateral toxic effects of antiblastic drugs].
Trattamento degli effetti tossici collaterali secondari da farmaci antiblastici.
AUTHOR: Pipino G; Raffaglio E
SOURCE: Minerva medica, (1967 Dec 15) 58 (100) 4576-8.
Journal code: 0400732. ISSN: 0026-4806.
PUB. COUNTRY: Italy

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196804
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19680410
CONTROLLED TERM: Adrenal Glands
***Antineoplastic Agents: AE, adverse effects**
Asthenia: DT, drug therapy
Headache: DT, drug therapy
Humans
Hypotension: DT, drug therapy
Nausea: DT, drug therapy
Neoplasms: DT, drug therapy
***Pyridoxine: TU, therapeutic use**
*Tissue Extracts: TU, therapeutic use
Vertigo: DT, drug therapy
CAS REGISTRY NO.: **65-23-6 (Pyridoxine)**
CHEMICAL NAME: 0 (**Antineoplastic** Agents); 0 (Tissue Extracts)

L219 ANSWER 42 OF 50 EMBASE
ACCESSION NUMBER: 2004147752 EMBASE
TITLE: Considerations concerning a tailored, individualized therapeutic management of patients with (neuro)endocrine tumours of the gastrointestinal tract and pancreas.
AUTHOR: De Herder W.W.; Krenning E.P.; Van Eijck C.H.J.; Lamberts S.W.J.
CORPORATE SOURCE: W.W. De Herder, Department of Internal Medicine, Section of Endocrinology, Erasmus MC, Dr Molewaterplein 40, 3015 GD Rotterdam, Netherlands. w.w.deherder@erasmusmc.nl
SOURCE: Endocrine-Related Cancer, (2004) Vol. 11, No. 1, pp. 19-34.
Refs: 177
ISSN: 1351-0088 CODEN: ERCAE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040429
Last Updated on STN: 20040429

ABSTRACT: Endocrine tumours of the gastrointestinal tract and pancreas may present at different disease stages with either hormonal or hormone-related symptoms/syndromes, or without hormonal symptoms. They may occur either sporadically or as part of hereditary syndromes. In the therapeutic approach to a patient with these tumours, excessive hormonal secretion and/or its effects should always be controlled first. Tumour-related deficiencies or disorders should also be corrected. Subsequently, control should be aimed at the tumour growth. Surgery is generally considered as first-line therapy for patients with localized disease, as it can be curative. However, in patients with metastatic disease the role of first-line surgery is not clearly established and other therapies should be considered, such as non-surgical cytoreductive therapies, biotherapy (with somatostatin analogues or interferon-α), embolization and chemoembolization of liver metastases, chemotherapy (with single or multiple dose regimens) and peptide

receptor-targeted radiotherapy. The delicate balance of the use of the different therapeutical options in patients with endocrine tumours of the gastrointestinal tract and pancreas emphasizes the importance of team approach and team expertise.

CONTROLLED TERM: Medical Descriptors:
*neuroendocrine tumor: DT, drug therapy
*neuroendocrine tumor: RT, radiotherapy
*neuroendocrine tumor: SU, surgery
*neuroendocrine tumor: TH, therapy
*pancreas islet cell tumor: DT, drug therapy
*gastrointestinal tumor: DT, drug therapy
symptom
treatment planning
hormone release
cancer control
tumor growth
metastasis: CO, complication
metastasis: SU, surgery
cancer patient
cancer therapy
artificial embolism
chemoembolization
dose response
cancer surgery
cancer combination chemotherapy
drug potentiation
side effect: SI, side effect
drug megadose
drug mechanism
antineoplastic activity
myelodysplastic syndrome: SI, side effect
acute granulocytic leukemia: SI, side effect
kidney failure: SI, side effect
human
clinical trial
review
Drug Descriptors:
*octreotide: DT, drug therapy
*octreotide: IM, intramuscular drug administration
*octreotide: SC, subcutaneous drug administration
*angiopeptin: DT, drug therapy
*angiopeptin: IM, intramuscular drug administration
*angiopeptin: SC, subcutaneous drug administration
***antineoplastic agent: AE, adverse drug reaction**
*antineoplastic agent: CB, drug combination
*antineoplastic agent: DT, drug therapy
somatostatin derivative: AE, adverse drug reaction
somatostatin derivative: CT, clinical trial
somatostatin derivative: CB, drug combination
somatostatin derivative: IT, drug interaction
somatostatin derivative: DT, drug therapy
somatostatin derivative: IM, intramuscular drug administration
somatostatin derivative: SC, subcutaneous drug administration
alpha interferon: CB, drug combination
alpha interferon: IT, drug interaction
alpha interferon: DT, drug therapy
proton pump inhibitor: CB, drug combination

proton pump inhibitor: DO, drug dose
proton pump inhibitor: DT, drug therapy
histamine H2 receptor antagonist: CB, drug combination
histamine H2 receptor antagonist: DO, drug dose
histamine H2 receptor antagonist: DT, drug therapy
diazoxide: DT, drug therapy
glucose: DT, drug therapy
insulin: DT, drug therapy
oral antidiabetic agent: DT, drug therapy
oral antidiabetic agent: PO, oral drug administration
loperamide: CB, drug combination
loperamide: DT, drug therapy
ondansetron: CB, drug combination
ondansetron: DT, drug therapy
ketoconazole: CB, drug combination
ketoconazole: DT, drug therapy
metyrapone: CB, drug combination
metyrapone: DT, drug therapy
etomidate: CB, drug combination
etomidate: DT, drug therapy
nicotinic acid: DT, drug therapy
zinc: DT, drug therapy
zinc: PO, oral drug administration
zinc: TP, topical drug administration
acetylsalicylic acid: DT, drug therapy
streptozocin: CB, drug combination
streptozocin: DT, drug therapy
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
etoposide: CB, drug combination
etoposide: DT, drug therapy
cisplatin: CB, drug combination
cisplatin: DT, drug therapy
(3 iodobenzyl)guanidine i 123: DT, drug therapy
radiopharmaceutical agent: AE, adverse drug reaction
radiopharmaceutical agent: CT, clinical trial
radiopharmaceutical agent: DT, drug therapy
pentetreotide in 111: DO, drug dose
pentetreotide in 111: DT, drug therapy
1,4,7,10 tetraazacyclododecane 1,4,7,10 tetraacetic acid
octreotide[3 tyrosine] y 90: AE, adverse drug reaction
1,4,7,10 tetraazacyclododecane 1,4,7,10 tetraacetic acid
octreotide[3 tyrosine] y 90: CT, clinical trial
1,4,7,10 tetraazacyclododecane 1,4,7,10 tetraacetic acid
octreotide[3 tyrosine] y 90: DT, drug therapy
unclassified drug
somatuline pr

CAS REGISTRY NO.: (octreotide) 83150-76-9; (angiopeptin) 113294-82-9; (diazoxide) 364-98-7; (glucose) 50-99-7, 84778-64-3; (insulin) 9004-10-8; (loperamide) 34552-83-5, 53179-11-6; (ondansetron) 103639-04-9, 116002-70-1, 99614-01-4; (ketoconazole) 65277-42-1; (metyrapone) 22752-91-6, 2405-72-3, 54-36-4, 908-35-0; (etomidate) 15301-65-2, 33125-97-2, 51919-80-3; (nicotinic acid) 54-86-4, 59-67-6; (zinc) 7440-66-6; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (streptozocin) 18883-66-4; (fluorouracil) 51-21-8; (doxorubicin) 23214-92-8, 25316-40-9; (etoposide) 33419-42-0; (cisplatin)

15663-27-1, 26035-31-4, 96081-74-2; ((3 iodobenzyl)guanidine i 123) 76924-93-1; (pentetreotide in 111) 139096-04-1
CHEMICAL NAME: (1) Sandostatin; (2) Sandostatin lar; (3) Somatuline; (4) Somatuline pr
COMPANY NAME: (2) Novartis (Switzerland); (4) Beaufour Ipsen

L219 ANSWER 43 OF 50 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003102756 EMBASE
TITLE: Developments in radiotherapy and adjuvant chemotherapy for head and neck cancer.
AUTHOR: Glaholm J.; Watkinson J.C.
CORPORATE SOURCE: Dr. J. Glaholm, Cancer Ctr. The Qu. Elizabeth Hosp., Univ. Hospital Birmingham NHS Trust, Birmingham B15 2TH, United Kingdom
SOURCE: Clinical Otolaryngology and Allied Sciences, (2003) Vol. 28, No. 1, pp. 1-4.
Refs: 38
ISSN: 0307-7772 CODEN: COTSD2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 011 Otorhinolaryngology
014 Radiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 20030325
Last Updated on STN: 20030325
CONTROLLED TERM: Medical Descriptors:
*head and neck cancer: DT, drug therapy
*head and neck cancer: RT, radiotherapy
*head and neck cancer: TH, therapy
*cancer radiotherapy
***cancer adjuvant therapy**
radiation dose fractionation
time
radiation exposure
cancer control
cancer survival
mucosa inflammation: CO, complication
radiation dose
tissue injury: CO, complication
disease severity
hypoxic cell
sensitization
cell hypoxia
radiosensitivity
hyperbaric oxygen
neurotoxicity: SI, side effect
larynx carcinoma: DT, drug therapy
larynx carcinoma: RT, radiotherapy
pharynx carcinoma: DT, drug therapy
pharynx carcinoma: RT, radiotherapy
drug tolerability
hypoxia: DT, drug therapy
metastasis: DT, drug therapy
metastasis: RT, radiotherapy
hypopharynx cancer: DT, drug therapy

hypopharynx cancer: RT, radiotherapy
cancer risk
human
nonhuman
clinical trial
editorial
priority journal
Drug Descriptors:
nitroimidazole derivative: AE, adverse drug reaction
nitroimidazole derivative: CT, clinical trial
nitroimidazole derivative: DO, drug dose
nitroimidazole derivative: DT, drug therapy
nitroimidazole derivative: PD, pharmacology
misonidazole: AE, adverse drug reaction
misonidazole: CT, clinical trial
misonidazole: DO, drug dose
misonidazole: DT, drug therapy
misonidazole: PD, pharmacology
etanidazole: AE, adverse drug reaction
etanidazole: CT, clinical trial
etanidazole: DO, drug dose
etanidazole: DT, drug therapy
etanidazole: PD, pharmacology
nimorazole: CT, clinical trial
nimorazole: DT, drug therapy
tirapazamine
carbogen: DT, drug therapy
carbogen: IH, inhalational drug administration
nicotinamide: DT, drug therapy
nicotinamide: PD, pharmacology
platinum derivative: DT, drug therapy
taxane derivative: DT, drug therapy
CAS REGISTRY NO.: (misonidazole) 13551-87-6; (etanidazole) 22668-01-5; (nimorazole) 6506-37-2; (tirapazamine) 27314-97-2; (carbogen) 8063-77-2; (nicotinamide) 11032-50-1, 98-92-0

L219 ANSWER 44 OF 50 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003096202 EMBASE
TITLE: Interactions between ionizing radiation and drugs in head and neck cancer: How can we maximize the therapeutic index?.
AUTHOR: Harrington K.J.; Nutting C.M.
CORPORATE SOURCE: K.J. Harrington, Targeted Therapy Laboratory, Cancer Res. UK Ctr. for Cell/Molec., Institute of Cancer Research, 237 Fulham Road, London SW3 6JB, United Kingdom. kevinh@icr.ac.uk
SOURCE: Current Opinion in Investigational Drugs, (1 May 2002) Vol. 3, No. 5, pp. 807-811.
Refs: 57
ISSN: 1472-4472 CODEN: CIDREE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 014 Radiology
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 20030325

Last Updated on STN: 20030325

CONTROLLED TERM: Medical Descriptors:
*head and neck cancer: RT, radiotherapy
*head and neck cancer: DT, drug therapy
human
clinical trial
meta analysis
ionizing radiation
cancer staging
cancer adjuvant therapy
radiation dose fractionation
treatment outcome
cancer chemotherapy
drug mechanism
radiosensitization
radiation protection
radiation response
probability
cancer control
cytotoxicity
radiological parameters
cancer mortality
drug efficacy
cancer risk
mucosa inflammation: SI, side effect
skin manifestation: SI, side effect
cancer radiotherapy
clinical protocol
therapy resistance
cell hypoxia
nausea and vomiting: SI, side effect
neuropathy: SI, side effect
squamous cell carcinoma: DT, drug therapy
drug targeting
cancer growth
receptor blocking
drug response
tumor vascularization
gene therapy
note
Drug Descriptors:
cytotoxic agent: DT, drug therapy
cytotoxic agent: PD, pharmacology
cytotoxic agent: AE, adverse drug reaction
cytotoxic agent: CB, drug combination
cisplatin: DT, drug therapy
cisplatin: CB, drug combination
taxane derivative: DT, drug therapy
taxane derivative: PD, pharmacology
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
docetaxel: DT, drug therapy
docetaxel: PD, pharmacology
irinotecan: DT, drug therapy
irinotecan: PD, pharmacology
gemcitabine: DT, drug therapy
gemcitabine: PD, pharmacology
recombinant erythropoietin: DT, drug therapy
nicotinamide: DT, drug therapy
carbogen: DT, drug therapy

nitroimidazole: DT, drug therapy
nitroimidazole: PD, pharmacology
nitroimidazole: AE, adverse drug reaction
bioreductive drug: DT, drug therapy
bioreductive drug: PD, pharmacology
bioreductive drug: CB, drug combination
mitomycin C: DT, drug therapy
mitomycin C: PD, pharmacology
tirapazamine: DT, drug therapy
tirapazamine: CB, drug combination
tirapazamine: PD, pharmacology
1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8
dihydroxyanthraquinone: DT, drug therapy
drug vehicle: DT, drug therapy
drug vehicle: CT, clinical trial
drug vehicle: PD, pharmacology
drug vehicle: AE, adverse drug reaction
liposome: DT, drug therapy
liposome: CT, clinical trial
liposome: PD, pharmacology
polymer: DT, drug therapy
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
monoclonal antibody: CT, clinical trial
monoclonal antibody: AE, adverse drug reaction
antibody conjugate: DT, drug therapy
antibody conjugate: PD, pharmacology
doxorubicin: DT, drug therapy
doxorubicin: AE, adverse drug reaction
epidermal growth factor receptor monoclonal antibody: DT, drug therapy
epidermal growth factor receptor monoclonal antibody: AE, adverse drug reaction
epidermal growth factor receptor monoclonal antibody: CT, clinical trial
epidermal growth factor receptor monoclonal antibody: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: AE, adverse drug reaction
cetuximab: DT, drug therapy
monoclonal antibody ICR 62: CT, clinical trial
monoclonal antibody ICR 62: AE, adverse drug reaction
monoclonal antibody ICR 62: DT, drug therapy
monoclonal antibody ICR 62: PD, pharmacology
gefitinib: DT, drug therapy
gefitinib: CT, clinical trial
gefitinib: PD, pharmacology
monoclonal antibody ABX EGF: DT, drug therapy
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
vasculotropin: EC, endogenous compound
unindexed drug
unclassified drug
imc c 225

CAS REGISTRY NO.: (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (paclitaxel) 33069-62-4; (docetaxel) 114977-28-5; (irinotecan) 100286-90-6; (gemcitabine) 103882-84-4; (recombinant erythropoietin) 113427-24-0, 122312-54-3,

130455-76-4; (nicotinamide) 11032-50-1, 98-92-0; (carbogen) 8063-77-2; (nitroimidazole) 36877-68-6; (mitomycin C) 50-07-7, 74349-48-7; (tirapazamine) 27314-97-2; (1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8 dihydroxyanthraquinone) 136470-65-0; (doxorubicin) 23214-92-8, 25316-40-9; (cetuximab) 205923-56-4; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (vasculotropin) 127464-60-2

CHEMICAL NAME: (1) Aq 4n; (2) Aq 4n; (3) Aq 4n; (4) Imc c 225; (5) Imc c 225; (6) Imc c 225; (7) Iressa; (8) Su 5416; (9) Su 6668

COMPANY NAME: (1) BTG; (2) Cancer Research (United Kingdom); (3) De Montfort University; (4) Imclone; (5) Bristol Myers Squibb; (6) Merck KGaA; (7) Astra Zeneca; (9) Sugen; National Cancer Institute; Abgenix; Immunex; Oxigene

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ACCESSION NUMBER: 2002216335 EMBASE

TITLE: Paclitaxel in cancer therapy.

AUTHOR: Mekhail T.M.; Markman M.

CORPORATE SOURCE: Dr. M. Markman, Dept. of Hematology/Medical Oncology, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States. Mekhair@ccf.org

SOURCE: Expert Opinion on Pharmacotherapy, (2002) Vol. 3, No. 6, pp. 755-766.
Refs: 106
ISSN: 1465-6566 CODEN: EOPHF7

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20020708
Last Updated on STN: 20020708

ABSTRACT: The last decade witnessed the introduction of exciting new chemotherapeutic agents. Among these, paclitaxel emerged as one of the most powerful compounds. Paclitaxel promotes the polymerisation of tubulin, thereby causing cell death by disrupting the normal microtubule dynamics required for cell division and vital interphase processes. Mechanisms of acquired resistance to paclitaxel include alterations of tubulin structure and the amplification of membrane phosphoglycoproteins that function as drug-efflux pumps. **Toxicities** associated with paclitaxel include hypersensitivity reaction, **neurotoxicity** and haematological ***toxicities.*** **Toxicities** may be both dose- and schedule-dependent. Paclitaxel has activity against a broad band of tumour types, including breast, ovarian, lung, head and neck cancers. Paclitaxel also has activity in other malignancies that are refractory to conventional chemotherapy, including previously-treated lymphoma and small cell lung cancers and oesophageal, gastric endometrial, bladder and germ cell tumours. Paclitaxel is also active against AIDS-associated Kaposi's sarcoma.

CONTROLLED TERM: Medical Descriptors:
cancer chemotherapy
protein polymerization

cell death
microtubule
cell division
interphase
drug resistance
protein structure
protein function
drug transport
hypersensitivity reaction: DT, drug therapy
hypersensitivity reaction: SI, side effect
neurotoxicity: DT, drug therapy
neurotoxicity: SI, side effect
blood toxicity: SI, side effect
dose response
antineoplastic activity
breast cancer: DT, drug therapy
ovary cancer: DT, drug therapy
lung cancer: DT, drug therapy
head and neck cancer: DT, drug therapy
malignant neoplastic disease: DT, drug therapy
lymphoma: DT, drug therapy
esophagus cancer: DT, drug therapy
stomach cancer: DT, drug therapy
endometrium cancer: DT, drug therapy
bladder cancer: DT, drug therapy
germ cell tumor: DT, drug therapy
AIDS related complex: DT, drug therapy
Kaposi sarcoma: DT, drug therapy
drug structure
structure activity relation
drug efficacy
drug blood level
myalgia: DT, drug therapy
myalgia: PC, prevention
myalgia: SI, side effect
cardiotoxicity: DT, drug therapy
cardiotoxicity: SI, side effect
area under the curve
human
clinical trial
controlled study
review
Drug Descriptors:
***paclitaxel: AE, adverse drug reaction**
***paclitaxel: CT, clinical trial**
*paclitaxel: AN, drug analysis
*paclitaxel: CB, drug combination
*paclitaxel: CM, drug comparison
*paclitaxel: CR, drug concentration
*paclitaxel: DO, drug dose
*paclitaxel: IT, drug interaction
*paclitaxel: DT, drug therapy
*paclitaxel: PD, pharmacology
*paclitaxel: IV, intravenous drug administration
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: AN, drug analysis
antineoplastic agent: CB, drug combination
antineoplastic agent: CM, drug comparison
antineoplastic agent: CR, drug concentration

antineoplastic agent: DO, drug dose
antineoplastic agent: IT, drug interaction
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
antineoplastic agent: IV, intravenous drug administration
tubulin: EC, endogenous compound
glycoprotein: EC, endogenous compound
Vinca alkaloid: CM, drug comparison
Vinca alkaloid: PD, pharmacology
taxane derivative: AE, adverse drug reaction
taxane derivative: CT, clinical trial
taxane derivative: AN, drug analysis
taxane derivative: CB, drug combination
taxane derivative: CM, drug comparison
taxane derivative: CR, drug concentration
taxane derivative: DO, drug dose
taxane derivative: IT, drug interaction
taxane derivative: DT, drug therapy
taxane derivative: PD, pharmacology
taxane derivative: IV, intravenous drug administration
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: CM, drug comparison
docetaxel: DT, drug therapy
docetaxel: PD, pharmacology
antihistaminic agent: DT, drug therapy
hypertensive agent: DT, drug therapy
corticosteroid: DT, drug therapy
dexamethasone: DT, drug therapy
dexamethasone: IV, intravenous drug administration
cisplatin: AE, adverse drug reaction
cisplatin: CT, clinical trial
cisplatin: CB, drug combination
cisplatin: CM, drug comparison
cisplatin: IT, drug interaction
cisplatin: DT, drug therapy
cisplatin: IV, intravenous drug administration
amifostine: DT, drug therapy
glutamic acid: DT, drug therapy
pyridoxine: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
narcotic agent: DT, drug therapy
doxorubicin: AE, adverse drug reaction
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: CM, drug comparison
doxorubicin: DO, drug dose
doxorubicin: IT, drug interaction
doxorubicin: DT, drug therapy
epirubicin: IT, drug interaction
razoxane: DT, drug therapy
trastuzumab: AE, adverse drug reaction
trastuzumab: CB, drug combination
trastuzumab: CM, drug comparison
trastuzumab: DT, drug therapy
CONTROLLED TERM: Drug Descriptors:
trastuzumab: PD, pharmacology
anthracycline: AE, adverse drug reaction
anthracycline: CB, drug combination
anthracycline: DT, drug therapy

tamoxifen: CT, clinical trial
tamoxifen: CB, drug combination
tamoxifen: CM, drug comparison
tamoxifen: DT, drug therapy
tamoxifen: PD, pharmacology
cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination
cyclophosphamide: CM, drug comparison
cyclophosphamide: DT, drug therapy
cytotoxic agent: AE, adverse drug reaction
cytotoxic agent: CT, clinical trial
cytotoxic agent: CB, drug combination
cytotoxic agent: CM, drug comparison
cytotoxic agent: DO, drug dose
cytotoxic agent: DT, drug therapy
cytotoxic agent: PK, pharmacokinetics
cytotoxic agent: PD, pharmacology
platinum: CB, drug combination
platinum: DT, drug therapy
carboplatin: AE, adverse drug reaction
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: CM, drug comparison
carboplatin: DO, drug dose
carboplatin: DT, drug therapy
carboplatin: PK, pharmacokinetics
carboplatin: PD, pharmacology
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
gemcitabine: CT, clinical trial
gemcitabine: CB, drug combination
gemcitabine: DT, drug therapy
unindexed drug

CAS REGISTRY NO.: (paclitaxel) 33069-62-4; (docetaxel) 114977-28-5; (dexamethasone) 50-02-2; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (amifostine) 20537-88-6; (glutamic acid) 11070-68-1, 138-15-8, 56-86-0, 6899-05-4; (pyridoxine) 12001-77-3, **58-56-0, 65-23-6**, 8059-24-3; (doxorubicin) 23214-92-8, 25316-40-9; (epirubicin) 56390-09-1, 56420-45-2; (razoxane) 21416-67-1, 21416-87-5, 24584-09-6, 24613-06-7; (trastuzumab) 180288-69-1; (tamoxifen) 10540-29-1; (cyclophosphamide) 50-18-0; (platinum) 7440-06-4; (carboplatin) 41575-94-4; (fluorouracil) 51-21-8; (gemcitabine) 103882-84-4

CHEMICAL NAME: (1) Taxol

COMPANY NAME: (1) Bristol Myers Squibb (United States)

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ACCESSION NUMBER: 1998298325 EMBASE

TITLE: Antidiarrheal agents for the management of treatment-related diarrhea in cancer patients.

AUTHOR: Ippoliti C.

CORPORATE SOURCE: Dr. C. Ippoliti, Bone Marrow Transplant Department, M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, United States. cippolit@notes.mdacc.tmc.edu

SOURCE: American Journal of Health-System Pharmacy, (1 Aug 1998) Vol. 55, No. 15, pp. 1573-1580.
Refs: 81

ISSN: 1079-2082 CODEN: AHSPEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 014 Radiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19980924
Last Updated on STN: 19980924

ABSTRACT: The efficacy and use of antidiarrheal agents in patients with diarrhea associated with cancer treatments are reviewed. Diarrhea is common in cancer patients and may interfere with cancer treatment. Diarrhea may be induced by chemotherapy, radiation therapy, surgery, graft-versus-host disease (GVHD) or infection after bone marrow transplantation, and other causes. The general goal of antidiarrheal therapy is to reduce fluid loss in the stool by inhibiting intestinal secretion, promoting absorption, and decreasing intestinal motility. Antidiarrheal agents may be classified as intestinal transit inhibitors, intraluminal agents, proabsorptive agents, and antisecretory drugs. Opiate agonists are the most commonly used intestinal transit inhibitors; they can be effective in treating cancer treatment- related diarrheas but must be used cautiously. Intraluminal agents include clays, activated charcoal, and cholestyramine; these adsorbents and other binding resins can interfere with the absorption of orally administered antidiarrheals and other drugs and are unlikely candidates for use in most cases of diarrhea in cancer patients. Clonidine, a proabsorptive agent, should be used only in patients with secretory diarrhea refractory to opiate agonist treatment. Octreotide is an antisecretory drug that has shown considerable efficacy in clinical trials as a treatment for diarrhea caused by chemotherapy or GVHD; its use for radiation therapy-induced diarrhea, although not studied clinically, is nevertheless an option. In general, opiate agonists and octreotide appear to offer the most efficacy and flexibility. Opiate agonists and octreotide are effective agents for cancer treatment-related diarrhea.

CONTROLLED TERM: Medical Descriptors:
*diarrhea: CO, complication
*diarrhea: DT, drug therapy
*diarrhea: SI, side effect
cancer patient
radiation injury
postoperative complication
bone marrow transplantation
cancer chemotherapy
graft versus host reaction
drug efficacy
human
review
priority journal
Drug Descriptors:
*antidiarrheal agent: DT, drug therapy
*opiate agonist: DT, drug therapy
*octreotide: DT, drug therapy
*stomach secretion inhibitor: DT, drug therapy
*chloride channel blocking agent: DT, drug therapy
*calmodulin inhibitor: DT, drug therapy
antineoplastic agent: AE, adverse drug reaction
activated carbon: DT, drug therapy
colestyramine: DT, drug therapy

clonidine: DT, drug therapy
diphenoxylate: DT, drug therapy
loperamide: DT, drug therapy
opiate: DT, drug therapy
enkephalin derivative: DT, drug therapy
glucose: DT, drug therapy
amino acid derivative: DT, drug therapy
oral rehydration solution: DT, drug therapy
somatostatin: DT, drug therapy
berberine: DT, drug therapy
acetylsalicylic acid: DT, drug therapy
nicotinic acid: DT, drug therapy
ispagula: DT, drug therapy
bismuth: DT, drug therapy

CAS REGISTRY NO.: (octreotide) 83150-76-9; (activated carbon) 64365-11-3, 82228-96-4; (colestyramine) 11041-12-6, 58391-37-0; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (diphenoxylate) 3810-80-8, 915-30-0; (loperamide) 34552-83-5, 53179-11-6; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (glucose) 50-99-7, 84778-64-3; (somatostatin) 38916-34-6, 51110-01-1; (berberine) 2086-83-1, 633-65-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (nicotinic acid) 54-86-4, 59-67-6; (ispagula) 77462-61-4, 8063-16-9; (bismuth) 7440-69-9

L219 ANSWER 47 OF 50 EMBASE

ACCESSION NUMBER: 96280451 EMBASE
DOCUMENT NUMBER: 1996280451
TITLE: Bleomycin antibiotics and their role in cancer chemotherapy.
AUTHOR: Huang L.; Xie Y.; Lown J.W.
CORPORATE SOURCE: Department of Chemistry, University of Alberta,Edmonton, Alta. T6G 2G2, Canada
SOURCE: Expert Opinion on Therapeutic Patents, (1996) Vol. 6, No. 9, pp. 893-899.
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
052 Toxicology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 961112
Last Updated on STN: 961112

ABSTRACT: The bleomycins are a group of glycopeptide anticancer cytotoxic agents which have been used in the clinical treatment of several human malignancies as single or combination chemotherapy for over two decades. However, the risk of dose-dependent pulmonary toxicity, which ultimately results in pulmonary fibrosis, limits the scale of application. Meanwhile, the unique mechanism of the antitumour effects of bleomycins has also attracted considerable interest from biologists. Extensive studies at the molecular level have provided a guide to attempts to obviate the pulmonary toxicity. Recent progress made in the areas of drug delivery, electropermeabilisation and conjugate synthesis has provided valuable additional information to improve bleomycin chemotherapy. The patents and publications discussed in this review

are selected from those covering the period from 1992 to date based on a Chemical Abstracts search.

CONTROLLED TERM: Medical Descriptors:
***cancer chemotherapy**
*lung toxicity: PC, prevention
*lung toxicity: SI, side effect
*lung toxicity: DT, drug therapy
animal model
antineoplastic activity
clinical trial
drug administration
drug conjugation
drug mechanism
drug targeting
electrochemotherapy
electropermeabilization
human
lung fibrosis: DT, drug therapy
lung fibrosis: PC, prevention
lung fibrosis: SI, side effect
malignant neoplastic disease: DT, drug therapy
nonhuman
patent
review
pharmaceutics
drug delivery system
Drug Descriptors:
*antineoplastic antibiotic: PR, pharmaceutics
***antineoplastic antibiotic: AE, adverse drug reaction**
*antineoplastic antibiotic: DO, drug dose
*antineoplastic antibiotic: TO, drug toxicity
*antineoplastic antibiotic: DT, drug therapy
*antineoplastic antibiotic: PD, pharmacology
***bleomycin: AE, adverse drug reaction**
*bleomycin: DO, drug dose
*bleomycin: DT, drug therapy
*bleomycin: PR, pharmaceutics
*bleomycin: PD, pharmacology
*bleomycin: TO, drug toxicity
*bleomycin derivative: TO, drug toxicity
*bleomycin derivative: DV, drug development
*bleomycin derivative: DT, drug therapy
*bleomycin derivative: PD, pharmacology
*bleomycin derivative: PR, pharmaceutics
alpha tocopherol: DT, drug therapy
apafant: DT, drug therapy
ascorbic acid: DT, drug therapy
bleomycin a2
bleomycin b2
bombesin: DT, drug therapy
bombesin: PD, pharmacology
bropirimine: DT, drug therapy
glycopeptide: TO, drug toxicity
glycopeptide: AE, adverse drug reaction
glycopeptide: PD, pharmacology
glycopeptide: DT, drug therapy
glycopeptide: DO, drug dose
hydrolase: DT, drug therapy

liblomycin: PD, pharmacology
liblomycin: DV, drug development
liposome: PR, pharmaceutics
nicotinamide: DT, drug therapy
nicotinic acid: DT, drug therapy
pepleomycin
peptide derivative: DT, drug therapy
peptide derivative: DV, drug development
peptide derivative: PD, pharmacology
razoxane: DT, drug therapy
retinol: DT, drug therapy
tallysomycin: PD, pharmacology
tallysomycin: DV, drug development
taurine: DT, drug therapy
thrombocyte activating factor antagonist: DT, drug therapy

CAS REGISTRY NO.: (bleomycin) 11056-06-7; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (apafant) 105219-56-5; (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (bleomycin a2) 11116-31-7; (bleomycin b2) 9060-10-0; (bombesin) 31362-50-2; (bropirimine) 56741-95-8; (hydrolase) 9027-41-2; (liblomycin) 88266-67-5; (nicotinamide) 11032-50-1, 98-92-0; (nicotinic acid) 54-86-4, 59-67-6; (pepleomycin) 68247-85-8, 70384-29-1; (razoxane) 21416-67-1, 21416-87-5, 24584-09-6, 24613-06-7; (retinol) 68-26-8, 82445-97-4; (tallysomycin) 67995-68-0; (taurine) 107-35-7

CHEMICAL NAME: Icrf 187; Web 2086

COMPANY NAME: Taiho; Nippon kayaku; Rhone poulenc rorer; Basf

L219 ANSWER 48 OF 50 EMBASE

ACCESSION NUMBER: 96068908 EMBASE

DOCUMENT NUMBER: 1996068908

TITLE: Medical treatment of metastasizing carcinoid tumors.

AUTHOR: Arnold R.

CORPORATE SOURCE: Div. of Gastroenterology/Metabolism, Department of Internal Medicine, Philipps-University Marburg, Baldingerstrasse,D-35033 Marburg, Germany

SOURCE: World Journal of Surgery, (1996) Vol. 20, No. 2, pp. 203-207.
ISSN: 0364-2313 CODEN: WJSUDI

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 009 Surgery
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English; French; Spanish

ENTRY DATE: Entered STN: 960319
Last Updated on STN: 960319

ABSTRACT: Long-acting somatostatin analogs, such as octreotide, comprise the therapeutic modality of choice for the symptomatic relief of flush and diarrhea in patients with carcinoid syndrome. The sequelae of gastric acid hypersecretion in patients with gastrin-producing duodenal carcinoids (gastrinoma) are perfectly controlled by proton pump inhibitors. Anti-proliferative medical strategies to control the growth of metastatic carcinoid tumors include long-acting somatostatin analogs, interferon alpha, and the combination of the two. However, the success rate is less than 50%, and it is

questionable whether true tumor regression can be expected. Controlled prospective studies are mandatory to address the question whether interferon or somatostatin analogs or the combination of the two should be used as first-line medical strategies and if hepatic artery embolization in patients with liver metastases should be performed before beginning medical therapy. Chemotherapy, including etoposide and cisplatin, has been shown to be effective only for purely differentiated neuroendocrine carcinomas and not for slowly growing carcinoids.

CONTROLLED TERM: Medical Descriptors:
*carcinoid syndrome: DI, diagnosis
*carcinoid syndrome: DT, drug therapy
*carcinoid syndrome: ET, etiology
*carcinoid syndrome: CO, complication
*gastrinoma: DI, diagnosis
*gastrinoma: DT, drug therapy
*gastrinoma: ET, etiology
*liver metastasis: CO, complication
*liver metastasis: DT, drug therapy
alopecia: SI, side effect
bone marrow toxicity: SI, side effect
cancer hormone therapy
cancer immunotherapy
cancer inhibition
clinical feature
clinical trial
conference paper
diarrhea: SI, side effect
drug efficacy
human
hyperglycemia: SI, side effect
intravenous drug administration
multicenter study
oral drug administration
pellagra: DT, drug therapy
pellagra: CO, complication
phase 2 clinical trial
steatorrhea: SI, side effect
subcutaneous drug administration
thyrotoxicosis: SI, side effect
vomiting: SI, side effect
water intoxication: SI, side effect
zollinger ellison syndrome: ET, etiology
zollinger ellison syndrome: DI, diagnosis
Drug Descriptors:
*adenosine triphosphatase inhibitor: CT, clinical trial
*adenosine triphosphatase inhibitor: DT, drug therapy
*adenosine triphosphatase inhibitor: PD, pharmacology
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: DT, drug therapy
***antineoplastic agent: AE, adverse drug reaction**
*antineoplastic agent: DO, drug dose
*histamine h2 receptor antagonist: DT, drug therapy
*histamine h2 receptor antagonist: CT, clinical trial
*interferon: PD, pharmacology
*interferon: AE, adverse drug reaction
*interferon: CT, clinical trial
*interferon: CB, drug combination
*interferon: DO, drug dose

*interferon: DT, drug therapy
*somatostatin analog: PD, pharmacology
*somatostatin analog: DT, drug therapy
*somatostatin analog: DO, drug dose
*somatostatin analog: CB, drug combination
*somatostatin analog: CT, clinical trial
*somatostatin analog: AE, adverse drug reaction
alpha adrenergic receptor blocking agent: DT, drug therapy
alpha interferon: PD, pharmacology
alpha interferon: CB, drug combination
alpha interferon: CT, clinical trial
alpha interferon: AE, adverse drug reaction
alpha interferon: DT, drug therapy
alpha interferon: DO, drug dose
alpha2b interferon: AE, adverse drug reaction
alpha2b interferon: DO, drug dose
alpha2b interferon: CT, clinical trial
alpha2b interferon: CB, drug combination
alpha2b interferon: DT, drug therapy
alpha2b interferon: PD, pharmacology
angiopeptin: DT, drug therapy
angiopeptin: AE, adverse drug reaction
angiopeptin: PD, pharmacology
chlorozotocin: DT, drug therapy
cisplatin: CT, clinical trial
cisplatin: AE, adverse drug reaction
cisplatin: CB, drug combination
cisplatin: DO, drug dose
cisplatin: DT, drug therapy
cyproheptadine: DT, drug therapy
etoposide: DO, drug dose
etoposide: DT, drug therapy
etoposide: AE, adverse drug reaction
etoposide: CT, clinical trial
etoposide: CB, drug combination
fenclonine: DT, drug therapy
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
glucocorticoid: DT, drug therapy
histamine h1 receptor antagonist: DT, drug therapy
hydrogen potassium adenosine triphosphatase: EC, endogenous compound
lansoprazole: DT, drug therapy
loperamide: DT, drug therapy
methysergide: DT, drug therapy
nicotinic acid: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
octreotide: CB, drug combination
octreotide: AE, adverse drug reaction
octreotide: CT, clinical trial
octreotide: DO, drug dose
octreotide: DT, drug therapy
octreotide: PD, pharmacology
omeprazole: DT, drug therapy
phenothiazine derivative: DT, drug therapy
serotonin antagonist: DT, drug therapy
somatostatin: PD, pharmacology
somatostatin: DT, drug therapy
streptozocin: CB, drug combination
streptozocin: DT, drug therapy

unindexed drug
CAS REGISTRY NO.: (alpha2b interferon) 99210-65-8; (angiopeptin) 113294-82-9; (chlorozotocin) 54749-90-5, 58484-07-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (cyproheptadine) 129-03-3, 969-33-5; (etoposide) 33419-42-0; (fenclonine) 1991-78-2, 7424-00-2; (fluorouracil) 51-21-8; (lansoprazole) 103577-45-3; (loperamide) 34552-83-5, 53179-11-6; (methysergide) 16509-15-2, 361-37-5, 62288-72-6; (nicotinic acid) 54-86-4, 59-67-6; (octreotide) 83150-76-9; (omeprazole) 73590-58-6, 95510-70-6; (somatostatin) 38916-34-6, 51110-01-1; (streptozocin) 18883-66-4

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ACCESSION NUMBER: 91349833 EMBASE
DOCUMENT NUMBER: 1991349833
TITLE: [The current treatment of prostate cancer].
MODALITES ACTUELLES DU TRAITEMENT DU CANCER DE LA PROSTATE.
AUTHOR: Fourcade R.O.
CORPORATE SOURCE: Service d'Urologie, Centre Hospitalier d'Auxerre, 2, Boulevard de Verdun, 89011 Auxerre, France
SOURCE: Revue du Praticien - Medecine Generale, (1991) Vol. 5, No. 155, pp. 2545-2550.
ISSN: 0989-2737 CODEN: RPMGE2
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
014 Radiology
016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
ENTRY DATE: Entered STN: 920316
Last Updated on STN: 920316
CONTROLLED TERM: Medical Descriptors:
***cancer chemotherapy**
*prostate cancer: RT, radiotherapy
*prostate cancer: EP, epidemiology
*prostate cancer: SU, surgery
*prostate cancer: DI, diagnosis
*prostate cancer: DT, drug therapy
adult
aged
article
biopsy
blood toxicity: SI, side effect
digestive system function disorder
disease classification
disease course
hot flush: SI, side effect
human
intramuscular drug administration
intranasal drug administration
liver toxicity: SI, side effect
lung disease
male
metastasis
oral drug administration

orchiectomy
subcutaneous drug administration
drug administration
drug therapy
sustained release preparation
Drug Descriptors:
*antiandrogen: AE, adverse drug reaction
*antiandrogen: AD, drug administration
*antiandrogen: DT, drug therapy
aminoglutethimide: DT, drug therapy
buserelin: DT, drug therapy
buserelin: AD, drug administration
cyproterone: DT, drug therapy
cyproterone: AD, drug administration
cyproterone: AE, adverse drug reaction
cyproterone acetate
estramustine phosphate: AE, adverse drug reaction
estramustine phosphate: CB, drug combination
estramustine phosphate: DT, drug therapy
estrogen: AD, drug administration
estrogen: DT, drug therapy
estrogen: AE, adverse drug reaction
flutamide: CB, drug combination
flutamide: AE, adverse drug reaction
flutamide: DT, drug therapy
gonadorelin derivative: DT, drug therapy
gonadorelin derivative: AE, adverse drug reaction
goserelin: AD, drug administration
goserelin: DT, drug therapy
ketoconazole: DT, drug therapy
ketoconazole: AE, adverse drug reaction
leuprorelin: DT, drug therapy
leuprorelin: AD, drug administration
nicotinamide: DT, drug therapy
nicotinamide: AE, adverse drug reaction
nicotinamide: AD, drug administration
nilutamide
triptorelin: DT, drug therapy
triptorelin: AD, drug administration
elexine
unclassified drug

CAS REGISTRY NO.: (aminoglutethimide) 125-84-8; (buserelin) 57982-77-1; (cyproterone) 2098-66-0; (cyproterone acetate) 427-51-0; (estramustine phosphate) 4891-15-0; (flutamide) 13311-84-7; (goserelin) 65807-02-5; (ketoconazole) 65277-42-1; (leuprorelin) 53714-56-0, 74381-53-6; (nicotinamide) 11032-50-1, 98-92-0; (nilutamide) 63612-50-0; (triptorelin) 57773-63-4

CHEMICAL NAME: Zoladex; Decapeptyl; Enantone; Suprefact; Androcur; Anandron; Estracyt; Elexine

L219 ANSWER 50 OF 50 EMBASE

ACCESSION NUMBER: 90153438 EMBASE

DOCUMENT NUMBER: 1990153438

TITLE: [Gastrointestinal **side effects** caused by cytostatic treatment of gynaecological malignant tumours].
GASTROINTESTINALE NEBENWIRKUNGEN BEI DER ZYTOSTATISCHEN BEHANDLUNG GYNAKOLOGISCHER MALIGNOME.

AUTHOR: Lotze W.
CORPORATE SOURCE: Frauenklinik, Bezirkskrankenhauses, Puschkinstrasse 2-4,DDR-6100 Meiningen, Germany
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ABSTRACT: Gastrointestinal complaints are the most frequent side effects of antineoplastic chemotherapy behind the bone marrow depressions. Nearly all cytostatic drugs, favourably used treating gynaecological malignant tumours, show a high complication rates on the part of the digestive organs. Primary and secondary damages can be so serious that the continuation of an effective tumour therapy becomes impossible. Whereas mucous excitement and motility disturbances are caused by local toxicity of cytostatic drugs, on the other hand central and psychogenic factors are of essential importance concerning nausea and vomiting. Therefore all these side effects could not be treated effective antiemetics alone. Only by an ingenious combination of medical treatment, psychological guidance and appropriate nutrition complaints can be relieved so far that the patients quality of life is interfered as less as possible and that a sufficient compliance may be reached.

CONTROLLED TERM: Medical Descriptors:
*gynecologic cancer: DT, drug therapy
*nausea: DT, drug therapy
*nausea: SI, side effect
*stomach motility
*vomiting: DT, drug therapy
*vomiting: SI, side effect
human experiment
human
female
short survey
priority journal
drug therapy
side effect
Drug Descriptors:
*antiemetic agent: AE, adverse drug reaction
*antiemetic agent: DT, drug therapy
*antiemetic agent: CM, drug comparison
***antineoplastic agent: AE, adverse drug reaction**
***antineoplastic agent: DT, drug therapy**
***antineoplastic agent: CM, drug comparison**
***bendamustine: AE, adverse drug reaction**
*bendamustine: DT, drug therapy
***bleomycin: AE, adverse drug reaction**
*bleomycin: DT, drug therapy
***busulfan: AE, adverse drug reaction**
*busulfan: DT, drug therapy
***chlorambucil: AE, adverse drug reaction**
*chlorambucil: DT, drug therapy

*cisplatin: DT, drug therapy
***cisplatin: AE, adverse drug reaction**
***cyclophosphamide: AE, adverse drug reaction**
*cyclophosphamide: DT, drug therapy
***dacarbazine: AE, adverse drug reaction**
*dacarbazine: DT, drug therapy
***dactinomycin: AE, adverse drug reaction**
*dactinomycin: DT, drug therapy
*doxorubicin: DT, drug therapy
***doxorubicin: AE, adverse drug reaction**
***epirubicin: AE, adverse drug reaction**
*epirubicin: DT, drug therapy
***fluorouracil: AE, adverse drug reaction**
*fluorouracil: DT, drug therapy
chlorphenethazine
chlorpromazine
dexamethasone
diazepam
ifosfamide
levomepromazine
meclozine
methotrexate
methylprednisolone
metoclopramide
mitomycin
mitoxantrone
neuroleptic agent
nitrosourea
procarbazine
promazine
scopolamine

CAS REGISTRY NO.: (bendamustine) 16506-27-7, 3543-75-7; (bleomycin) 11056-06-7; (busulfan) 55-98-1; (chlorambucil) 305-03-3; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (cyclophosphamide) 50-18-0; (dacarbazine) 4342-03-4; (dactinomycin) 1402-38-6, 1402-58-0, 50-76-0; (doxorubicin) 23214-92-8, 25316-40-9; (epirubicin) 56390-09-1, 56420-45-2; (fluorouracil) 51-21-8; (chlorphenethazine) 2095-24-1, 22632-00-4; (chlorpromazine) 50-53-3, 69-09-0; (dexamethasone) 50-02-2; (diazepam) 439-14-5; (ifosfamide) 3778-73-2; (levomepromazine) 1236-99-3, 60-99-1, 7104-38-3; (meclozine) 1104-22-9, 36236-67-6, 569-65-3, **8054-07-7, 8064-07-1**; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (methylprednisolone) 6923-42-8, 83-43-2; (metoclopramide) 12707-59-4, 2576-84-3, 364-62-5, 7232-21-5; (mitomycin) 1404-00-8; (mitoxantrone) 65271-80-9, 70476-82-3; (nitrosourea) 13010-20-3; (procarbazine) 366-70-1, 671-16-9; (promazine) 53-60-1, 58-40-2; (scopolamine) 138-12-5, 51-34-3, 55-16-3

CHEMICAL NAME: Cerucal; Diadril; Elroquil; Faustan; Tisercin; Propaphenin; Sinophenin

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